Studies on the Reactivity of Titanocene Alkylidenes and Titanocene Alkyl Chlorides

Thesis by

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Finally, I would like to thank my family for their support and faith in me.

ABSTRACT

The scope and limitations of the reaction of titanocene methylidene with ketones were investigated. Easily enolizable ketones are methylenated quantitatively and isolated in high yield. This reagent also demonstrates chemoselectivity for ketones over esters and regioselectivity for less hindered ketones. Enolates are produced by proton transfer to the methylidene from very sterically (but not particularly acidic) ketones.

A simple one-pot method for the production of a geminal dimethylated center from a ketone and two equivalents of titanocene methylidene has been developed. This is a very sterically restricted process that is complementary to similar reactions using other organometallic reagents.

The heterocyclic compounds, benzothiazole and benzoxazole, react with titanocene methylidene, presumably to form aza-metallacycles, which then undergo a β-elimination to form novel metallacycles. This reaction is not general for other compounds with an X–C=N linkage (X=O, S).

Fundamental processes involved in Ziegler–Natta polymerization have been investigated in a homogeneous Ti/Al-based model system. Lewis acid catalyzed olefin insertion was studied with titanocene alkenyl chlorides. This reaction is irreversible. Deuterium-labelling experiments provide support for the direct insertion mechanism. The reverse process, β-alkyl elimination, was also examined with titanocene methylcyclobutyl chloride. This process is also irreversible with no competing β-hydrogen elimination.

NMR studies were performed to probe the nature of the interaction between titanocene alkenyl chlorides and alkyl aluminum chloride cocatalysts in the intramolecular olefin insertion. This system is a model for the active site in Ziegler–Natta polymerization. A Lewis acid concentration dependence on the reaction is observed. A possible explanation for this concentration dependence is presented.

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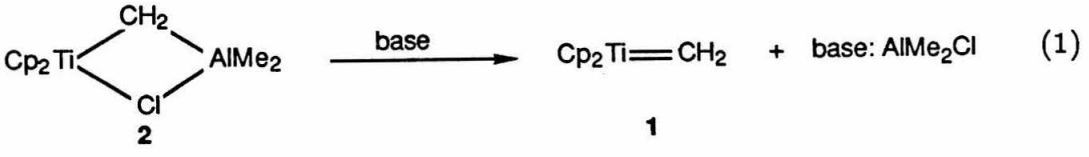
Chapter 1

The Scope and Limitations of the Reaction of Titanocene Methylidene with Ketones

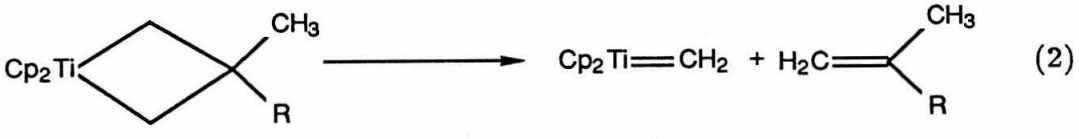
INTRODUCTION

Organotransition metal compounds are finding increasing acceptance for use as reagents in organic synthesis primarily because of their unusual reactivity patterns and high specificity. They are often able to induce unique and useful transformations to give products in superior yield and with greater selectivity than those obtained using other reagents.[1]

Organotitanium compounds make up an important class of these reagents.[2] Their use is becoming increasingly widespread in organic synthesis. A reagent that has been subject to a great deal of study is titanocene methylidene **1**. This reactive intermediate was first generated in the dissociation of dimethylaluminum chloride from the "Tebbe reagent"[3] **2**. (See Equation 1.) Titanocene methylidene can also be generated by the cleavage of β-substituted titanacyclobutanes **3**. (See Equation 2.) Titanocene methylydene was first studied in mechanistic experiments involving olefin metathesis, with **2** being a catalyst for metathesis and **1** and **3** being intermediates in this process.[4] Further research indicated that this reactive intermediate reacts with a wide variety of functional groups to produce synthetically useful products.[5]



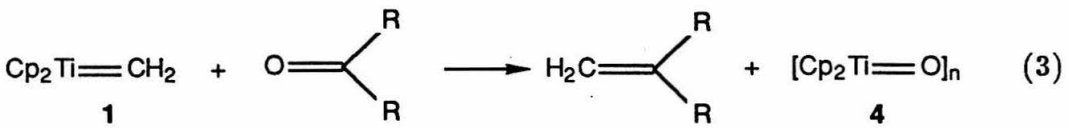
2 **1** (1)



3 **3a**: R = Me
3b: R = n-Pr

1 (2)

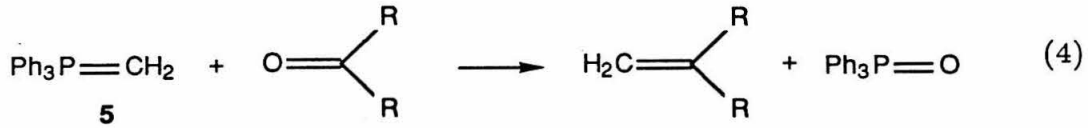
A great deal of study has concentrated on the reactivity of **1** with carbonyl containing compounds. With most of these substrates, the methylene group from **1** is transferred to the carbonyl carbon, producing a terminal alkene. (See Equation 3.) The nucleophilicity of the methylidene carbon and the oxophilicity of titanium make **1** a powerful "Wittig" type reagent. With ordinary ketones, this reaction proceeds rapidly and quantitatively. This transformation results in the formation of a carbon-carbon bond, unquestionably one of the most important classes of reactions in organic synthesis. Similar transformations using other ylides from metals such as zirconium,[6] tantalum,[7] niobium,[7] tungsten,[8] and most recently, uranium[9] have been reported.



(3)

The Wittig reaction,[10] using methylene triphenylphosphorane **4**, (see Equation 4) has been the most generally useful procedure for the synthesis of terminal olefins from carbonyl centers since its introduction over 30 years ago.[11] Over the years, many modifications have been introduced to expand the utility of this reaction. Significant modifications include use of the dimsyl anion in DMSO[12] and the α-lithiomethylene triphenylphosphorane[13] as means to effect methylenation in hindered or unreactive ketones.

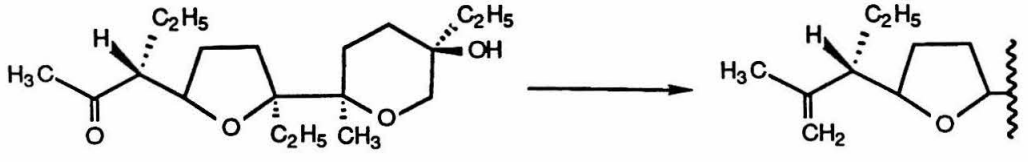
One goal in designing reagents for organic synthesis is the generation of reagents that provide transformations unattainable with classical reagents. As useful as the Wittig reaction is, the use of phosphorus ylides does have some limitations that have not yet been overcome.[11a] The use of **1** serves to *reduce some of*



(4)

the restrictions on this transformation; it has been used successfully as a methylene transfer agent on substrates such as esters under very mild conditions. This is of considerable interest because direct methylenation of esters using phosphorus ylides does not constitute a viable synthetic method.

Another attractive feature of titanocene methylidene is its nonbasic character relative to the rate of methylene transfer. Typical Wittig reagents can function as strong bases, removing the acidic α-hydrogens of some carbonyl compounds. Therefore, with ketones having very acidic α-hydrogens, proton abstraction becomes the dominant reaction, so that epimerization and condensation reactions are fast relative to methylene transfer.[11a] It has been observed that an optically active ketone with an α-chiral center can be rapidly methylenated with **1** without loss of optical activity.[14] (See Equation 5.)



(5)

$Cp_2Ti{=}CH_2$ 60-70% yield (rapid)---no isomerization of alpha-center

$Ph_3P{=}CH_2$ 20-30% yield (very slow)---mostly isomerized

In light of the results seen with optically active ketones, the possibility of methylene transfer to enolizable ketones appeared likely. The direct methylenation of these compounds is a desirable yet unattainable transformation with the more basic phosphorus ylides. The results reported in this chapter regarding the use of **1** to effect methylene transfer to enolizable ketones have been reported in a preliminary communication.[15]

This work and previous studies with **2** and **3** have shown that these reagents will react with a wide variety of organic substrates. However, when working with complex organic systems, it is important to be able to predict the reactivity of a reagent on a range of similar functional groups. A reagent's chemoselectivity increases its utility and value in organic synthesis, because selectivity allows for desired reactions to proceed without unwanted products or mixtures of products or undesired transformations on other functional groups. In addition to determining the chemoselectivity of **1**, we have also explored the regioselectivity and have determined the steric limitations of this reagent with ketones.

RESULTS AND DISCUSSION

Reaction of Titanocene Methylidene with Easily Enolizable Ketones

The typical Wittig reagents are basic enough for proton abstraction to compete with methylene transfer in some cases. The abstraction becomes particularly pronounced with easily enolizable cyclic ketones such as cyclohexanones and cyclopentanones. If the reaction between the ylide and the carbonyl compound is in any way sterically hindered, enolization becomes the main reaction,[11a] thus making these reagents ineffective as methylene sources. Table 1 lists the results of methylenation by titanocene methylidene of a number of such ketones with varying degrees of steric hindrance. All are quite rapidly methylenated and easily isolated in consistently high yield. Most of these reactions are quantitative by NMR.

The experimental conditions are general for most ketones as well as for aldehydes, esters, and lactones. This simple procedure involves treatment of the ketone substrate with a slight excess of **2** or **3** in THF or Et_2O at low temperature. The reaction mixture is allowed to warm to room temperature, followed by a simple workup and isolation. Both reagents appear to work equally well. The choice of **2** or **3** as a source of **1** is largely dictated by experimental convenience because yields are comparable for the two. For example, the Tebbe reagent is commercially available and can be used in the temperature range of −40 °C to room temperature. It is compatible with ethereal solvents at low temperature and aromatic hydrocarbons or dichloromethane at all temperatures. (The use of non-ethereal solvents requires the addition of one equivalent of a Lewis base such as pyridine to induce dissociation of dimethylaluminum chloride.) The major disadvantage of using the Tebbe reagent is that dimethylaluminum chloride or the aqueous workup may cause unwanted side reactions and other complications. On the other hand, the less Lewis acidic titanacyclobutanes can be easily prepared from **2** and the appropriate olefin. They react rapidly with ketones at about 5 °C or above and are

Table 1. Enolizable ketones and methylenation products

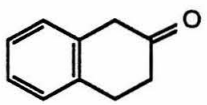
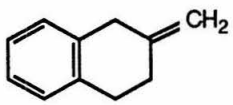
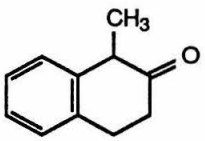
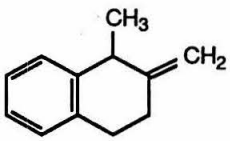
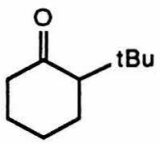
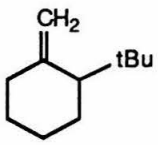
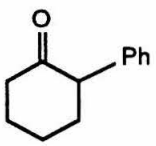
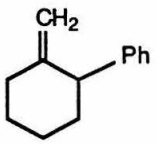
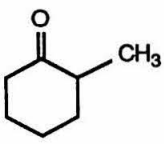
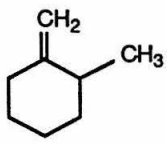
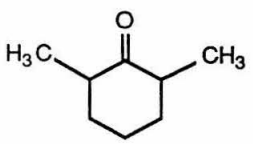
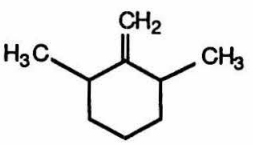
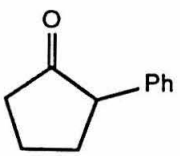
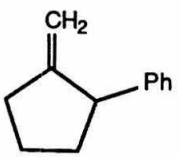
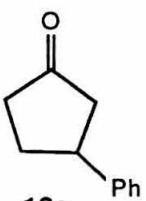
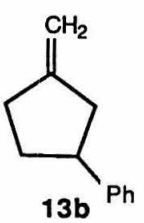
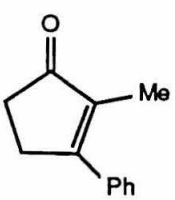
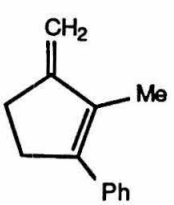
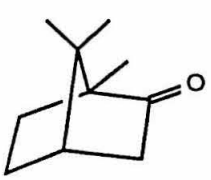
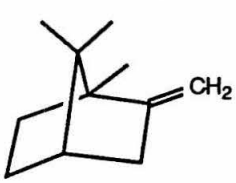
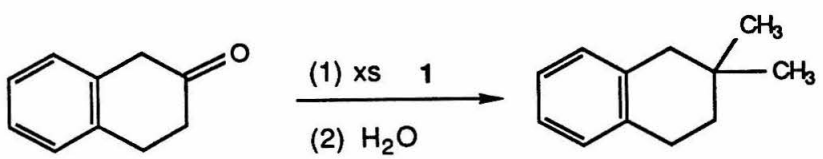
Ketone	Product	Yield	
		2	**3**
 **6a**	 **6b**	84	90
 **7a**	 **7b**	85	88
 **8a**	 **8b**	92	95
 **9a**	 **9b**	93	98
 **10a**	 **10b**	88	92

Table 1. (continued)

Ketone	Product	Yield	
		2	**3**
 **11a**	 **11b**	91	93
 **12a**	 **12b**	89	97
 **13a**	 **13b**	90	92
 **14a**	 **14b**	93	98
 **15a**	 **15b**	78	82

compatible with ethereal or aromatic solvents. The only side product observed is a titanocene oxo-polymer, $[Cp_2Ti{=}O]_n$ **4**, which is easily removed by precipitation with pentane and filtration. Passage of the semi-concentrated reaction mixture through a short pad of alumina or silica gel and concentration generally yields the pure alkene product. Again, the method of purification depends on the acid lability of the product.

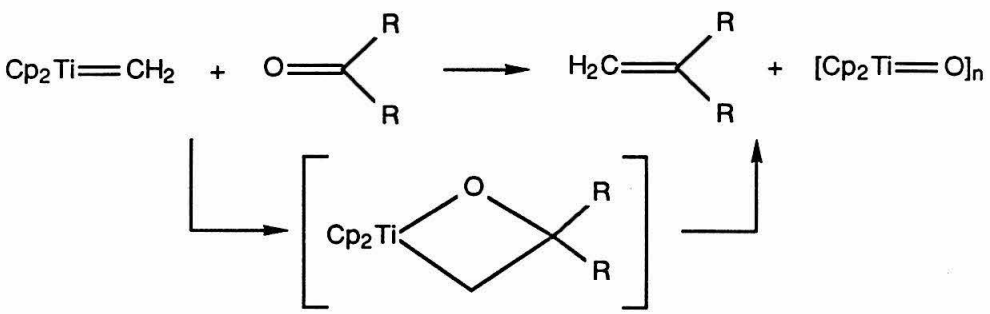
In only one of the ketones listed in Table 1, 2-tetralone **6a**, is it necessary to modify the reaction conditions. As will be discussed in Chapter 2, the methylenated product of this ketone **6b** forms a very stable metallacycle with titanocene methylidene. If there is any excess titanocene methylidene, this metallacycle is formed.[16] The aqueous workup of the reaction produces a dimethylated product. (See Equation 6.) Therefore, in order to isolate an alkene without the dimethylated side product, it is necessary to avoid an excess of **1** and to allow the reaction mixture to stir at room temperature for about an hour, so that any metallacycle formed will decompose before workup. Then the alkene can be isolated in high yield.



6a **6c** (6)

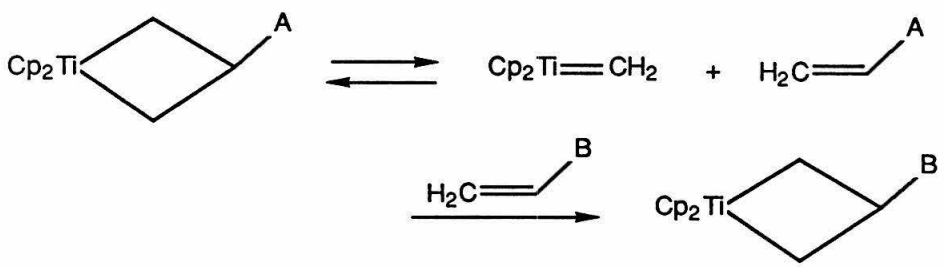
The proposed mechanism for the reaction of ketones with **2** or **3** is analogous to the one for olefin methathesis in which **1** is the actual reactive species. (See Scheme 1.) This mechanism involves an intermediate oxa-metallacycle **16** that cleaves to give titanocene oxo-polymer and the alkene product. The $Ti{=}O$ bond

Methylenation

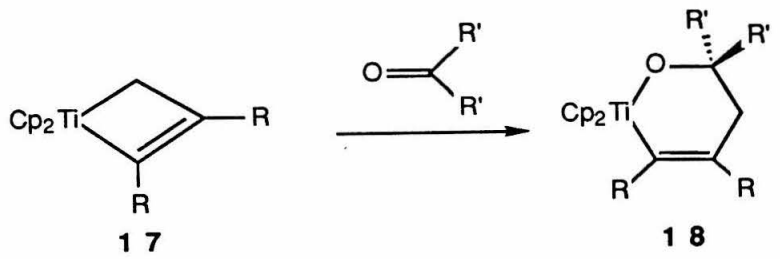


16

Olefin Metathesis



Scheme 1. Comparison of methylenation and olefin metathesis.

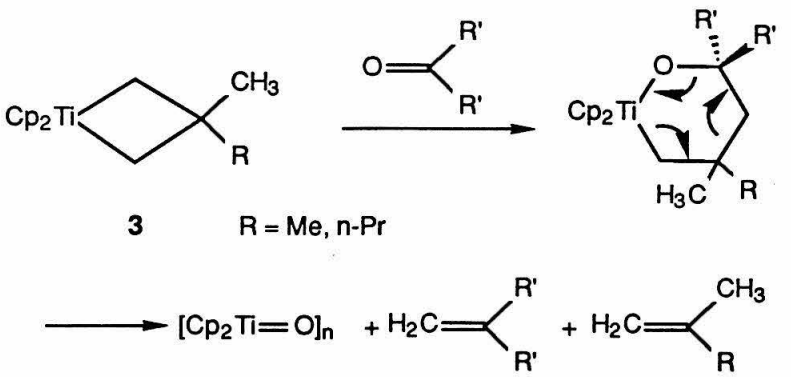


17 18 (7)

formed is an extremely strong one, giving the reaction a strong thermodynamic driving force.

Although the intermediate oxa-metallacycle has never been observed in a reaction between **1** and a ketone, this general mechanism is thought to be the correct one. However, alternative mechanisms have been raised. Work with titanocyclobutenes **17** show that ketones insert into a titanium-carbon bond to form titanoceneoxacyclohexenes **18**.[17] (See Equation 7.) In this reaction, the products are stable, but in the case with titanacyclobutanes, one might envision a similar 6-membered ring intermediate that reacts further to give the observed products. (See Equation 8.) Results reported herein and in earlier reports are not consistent with this mechanism. In addition to the titanacyclobutanes used in this work, a number of others have been prepared with **2** and various olefins. Equilibrium studies[18] have shown that the stability of these metallacycles depends on the substitution pattern, giving each one a characteristic temperature at which it will undergo olefin metathesis, that is, cleave to **1** and olefin. Ketones will react only with a particular metallacycle above the temperature at which it has been shown to undergo metathesis. While it is not expected that all ketones would react with all metallacycles at the same temperature, the fact that the "metathesis temperature" and the "methylene transfer temperature" are identical argues strongly against the mechanism outlined in Equation 8.

Alternate methylenation mechanism

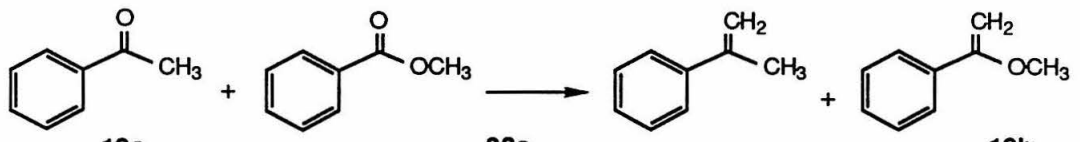


(8)

Chemoselectivity of Titanocene Methylidene for Ketones over Esters

In order to assess the relative reactivities of esters and ketones toward titanocene methylidene, competition experiments were performed using various substrates. In the first experiment, a solution of 1 mmol each of methyl benzoate and acetophenone was added to a solution of 1 mmol of **3** in toluene, using reaction conditions identical to those used with the ketones in Table 1. Analysis of the reaction mixtures by capillary gas chromatography showed an 89:11 ratio of β-methyl styrene **19a** to β-methoxy styrene **20a**. The same experiment was performed with **2**, again using these standard reaction conditions. This reagent proved to be more selective, providing a 97:3 ratio of **19b** to **20b**. This ratio can be increased further by slowly adding the solution of **2** to the substrates at -40 °C. Under these conditions, methylenation of acetophenone was seen exclusively. These competition experiments were repeated using several equivalents (2-10) of each of the carbonyl substrates per equivalent of **1** source. The average product ratios are listed in Table 2.

Table 2. Product ratios from chemoselectivity experiments (acetophenone vs. methyl benzoate)



19a **20a** **19b**

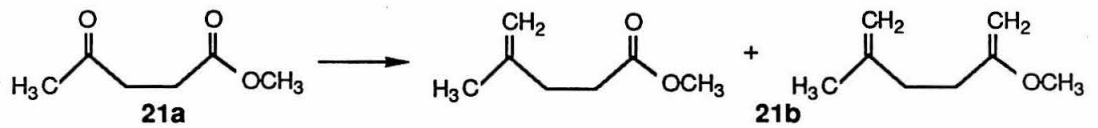
source of 1		
3	89	11
2	97	3
2*	100	0

*Tebbe reagent with modified reaction conditions

These experiments were repeated using ethyl levulinate **21a**, a compound having both ketone and ester moieties. In the reaction with **3**, under standard reaction conditions, products formed from single and double methylenation (**21b:21c**) are formed in a ratio of 85:15. Again, **2** exhibits greater selectivity than **3**. The results of these experiments are listed in Table **3**.

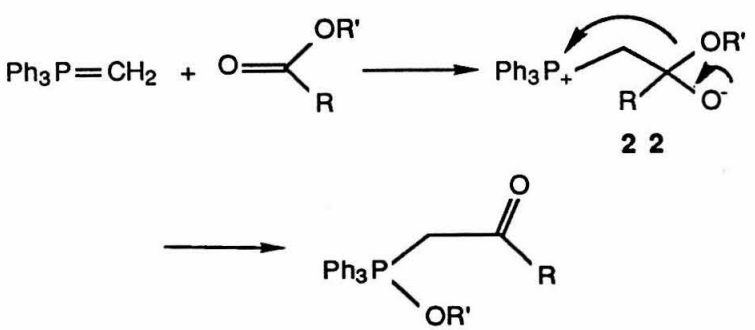
The results from these competition experiments show that **1** demonstrates quite high selectivity for ketones over esters. Similar results have also since been reported by other workers.[19] The carbonyl carbon of the ester is less electrophilic,[20] slowing nucleophilic attack by the methylidene. This is consistent with other reactions involving nucleophilic attack on a carbonyl group. Additionally, esters are slightly weaker bases than ketones,[21] slowing the presumed coordination of the carbonyl oxygen to the electrophilic and oxophilic metal center. This coordination

Table 3. Product ratios from chemoselectivity experiments (ethyl levulinate)



source of 1		
3	85	15
2	97	3
2*	100	0

*Tebbe reagent with modified reaction conditions



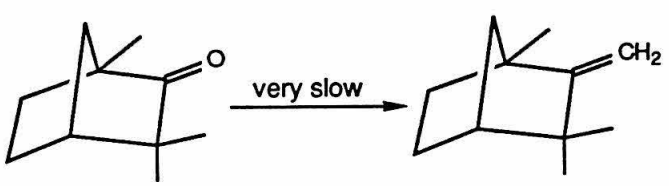
(9)

may be responsible for the fact that **1** will methylenate esters, while phosphorus ylides will not. As discussed earlier, the reaction of **1** with carbonyl compounds is presumed to proceed *via* an intermediate metallacycle that cleaves to form prod-

ucts. On the other hand, when treated with esters, phosphorus ylides react to form an intermediate betaine **22** by a simple nucleophilic attack.[22] (See Equation 9.) The betaine intermediate then eliminates the β-alkoxide substituent. There appears to be no significant interaction between the phosphorus and the carbonyl oxygen. However, with **1**, no β-alkoxide elimination has been observed in reactions with esters; only enol ether products are produced. This can be attributed to a strong Ti–O interaction in the oxa-metallacycle, which irreversibly eliminates $[Cp_2Ti{=}O]_n$. The strong interaction of the oxygen with the metal center precludes β-alkoxide elimination.

Regioselectivity of Titanocene Methylidene

A reagent's usefulness can also be extended by a demonstration of regioselectivity. After determining the chemoselectivity of titanocene methylidene, we were interested in determining the regioselectivity for methylene transfer to ketones in different steric environments. It had been noted previously that the reaction with the very sterically hindered ketone, ℓ-fenchone **23**, was extremely slow. (See Equation 10.) It is so slow, in fact, that in the reaction with **2**, decomposition of the titanium reagent competes effectively with methylene transfer, so that no olefin product is produced. The use of **3** as the methylenating agent gives up to 20% conversion to the terminal olefin. This result alluded to the regioselectivity with this reagent.

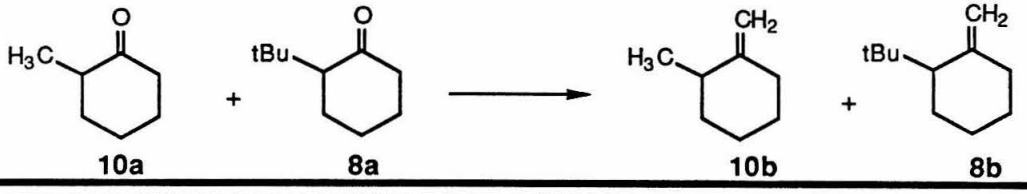


23 (10)

Competition experiments were performed with variously substituted cyclohexanones. These experiments were similar to those described previously. Because of the increase of chemoselectivity seen when using **2** at low temperature, these competition experiments were performed with **2** only.

The first set of ketones used were 2-methylcyclohexanone **10a** and 2-*tert*-butylcyclohexanone **8a**. Under the standard reaction conditions, a preference of the methyl-substituted ketone was observed, the ratio of products being 2:1. Again this selectivity was increased somewhat by the addition of a solution of **2** to the ketones at −40 °C. This gave a ratio of approximately 5:1, favoring the ketone with the smaller substituent. (See Table 4.)

Table 4. Product ratios from regioselectivity experiments (2-methylcyclohexanone vs. 2-t-butylcyclohexanone)



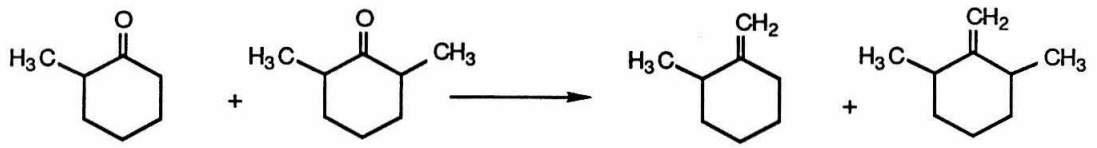
10a **8a** **10b** **8b**

source of 1		
2	2	1
2*	5	1

*Tebbe reagent with modified reaction conditions

A second set of competition experiments using cyclohexanones with a different substitution pattern was performed. The increased number of substituents led to greater selectivity. The ratio of products seen is approximately 10-12:1, favoring

Table 5. Product ratios from regioselectivity experiments (2-methylcyclohexanone vs. 2,6-dimethylcyclohexanone)



10a **11a** **10b** **11b**

source of 1		
2	6-7	1
2*	10-12	1

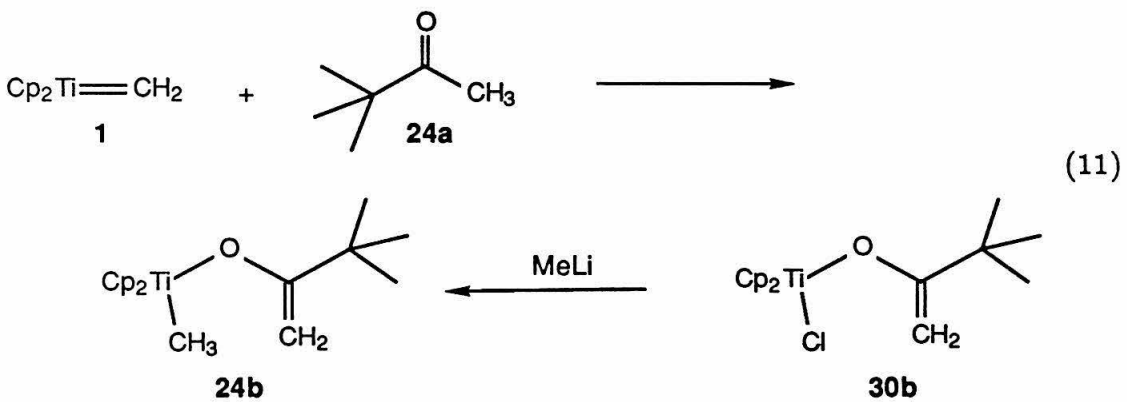
*Tebbe reagent with modified reaction conditions

the singly substituted 2-methylcyclohexanone **10a** over 2,6-dimethylcyclohexanone **11a**. In these experiments, the individual conditions have not been optimized, so the potential for greater selectivity remains. (See Table 5.)

Reactions with Very Sterically Hindered Ketones

Upon further investigation of the reactivity of **1** with ketones, it was discovered that **1** reacts quite differently when the ketone is very sterically hindered. This was first observed in an NMR tube reaction of **3** with pinacolone **24a**. Typically, these methylenation reactions are carried out in an NMR tube in melting benzene-d_6 and are normally complete within 1-2 min. The completion of the reaction is noted by the precipitation of $[Cp_2Ti{=}O]_n$. However, with this ketone, there was no precipitate. A very slight color change was the only evidence that any reaction had occurred. The NMR spectrum of the reaction mixture included a new sharp signal in the cyclopentadienyl region indicating an organometallic product, unusual for a reaction of **1** with a ketone. Other unusual signals were

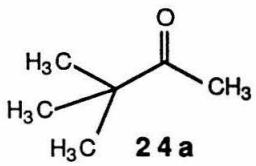
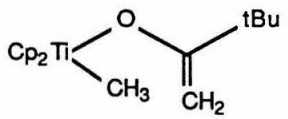
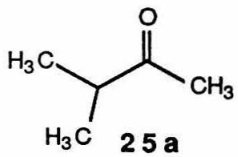
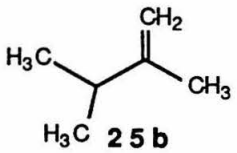
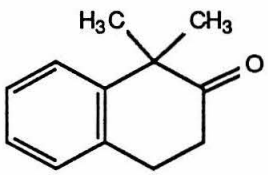
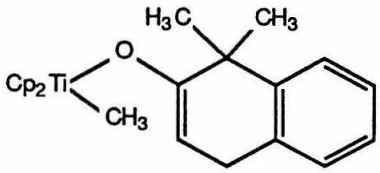
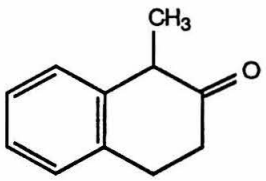
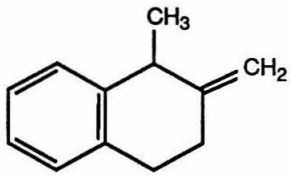
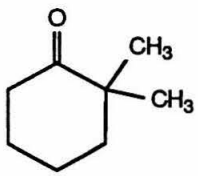
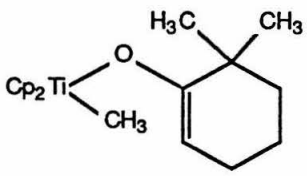
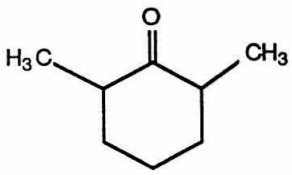
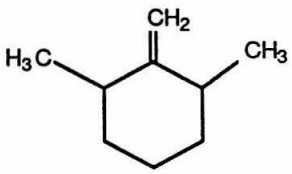
the singlets at 3.35 ppm and 3.86 ppm. These were too far upfield to be the signals anticipated for the expected terminal olefin product, which has signals in the range of 4.6-4.8 ppm. The singlets integrated as one proton each relative to the cyclopentadienyl signals. These high field signals are characteristic of titanocene chloride enolates.[23] (The chloride enolates are prepared by treating acid chlorides with **1**.[23,24]) Another singlet at 0.86 ppm, an apparent methyl group, led to the tentative identification of this compound as the titanocene methyl enolate of pinacolone. This assignment was verified by the independent preparation of **24b** by treating the titanocene chloride enolate of pinacolone **30b** with MeLi. (See Equation 11.) This reaction gave a red compound with an identical NMR spectrum.

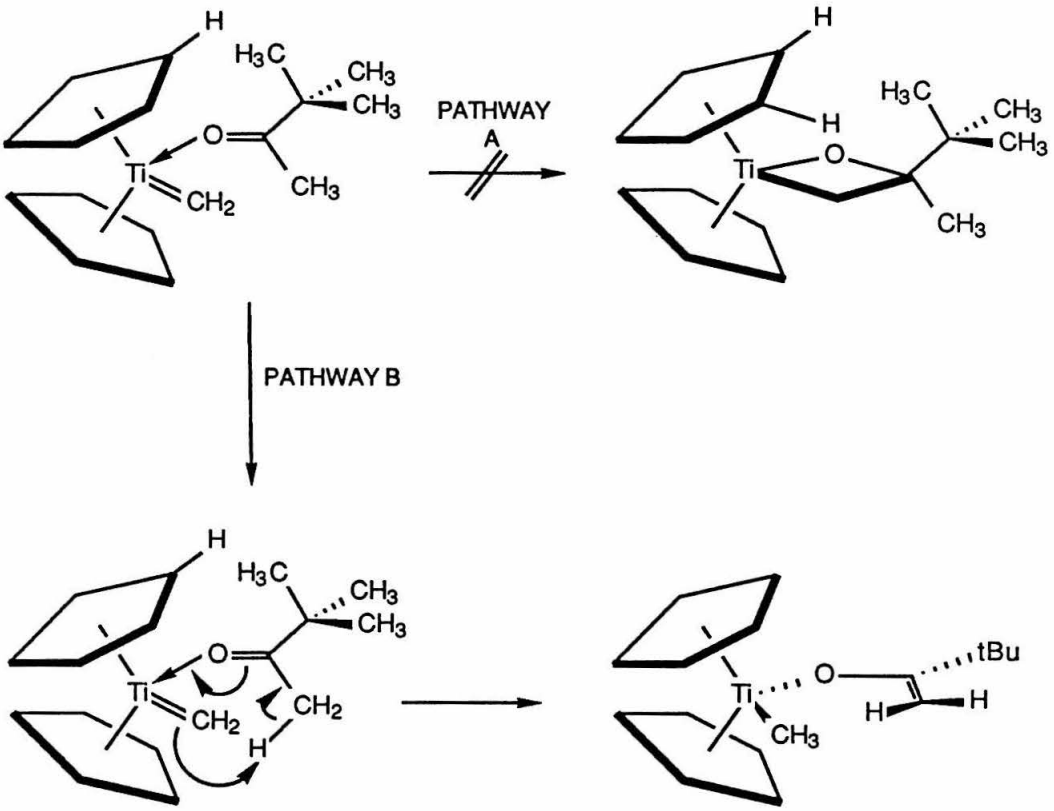


(11)

The formation of an enolate product initially appeared incongruous with earlier results of rapid methylene transfer to ketones *in spite* of their easy enolizability. Although it has been reported by Cannizzo[23] that the titanocene methylidene can be protonated by proton sources such as alcohols and carboxylic acids, it had always been assumed that the rate of methylene transfer to ketones was faster than that of proton transfer from ketones to the methylidene.

Table 6. Ketones with their respective reaction pathways and products

ketone	reaction pathway	product
 **24a**	**B**	 **24b**
 **25a**	**A**	 **25b**
 **26a**	**B**	 **26b**
 **7a**	**A**	 **7b**
 **27a**	**B**	 **27b**
 **28a**	**A**	 **28b**



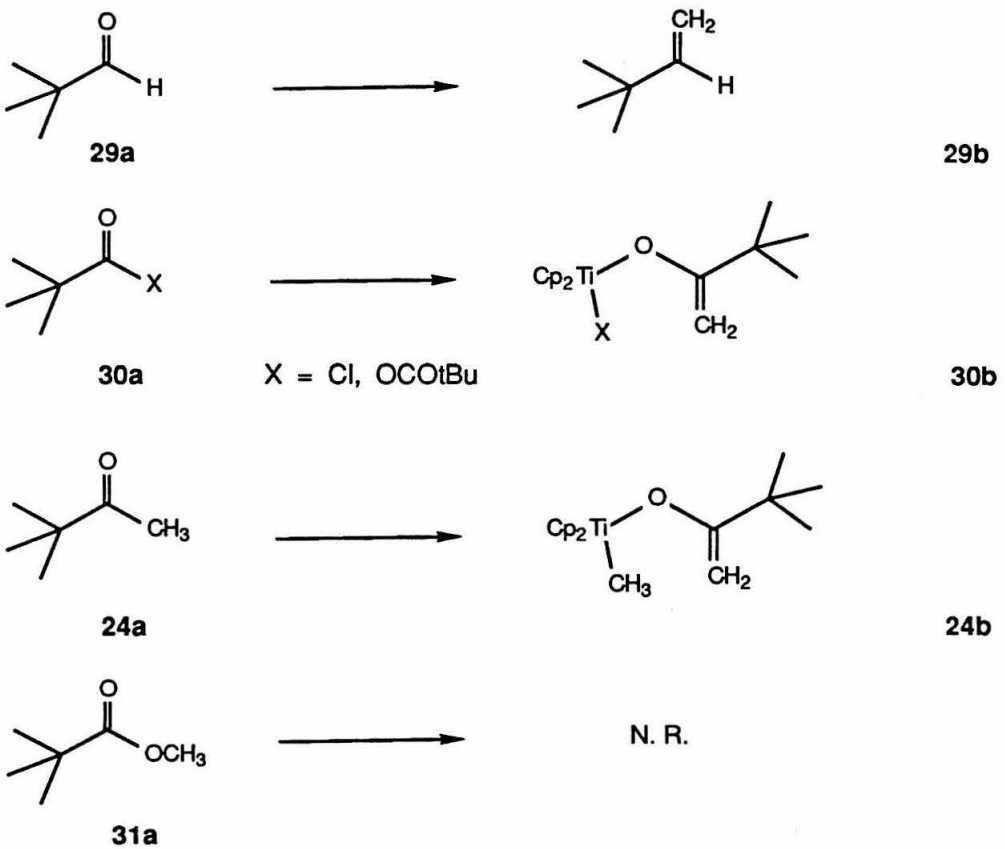
Scheme 2. Mechanism for proton transfer from hindered ketones to titanocene methylidene.

This result now demonstrates that with pinacolone and other ketones listed in Table 6, the steric bulk of the ketone can slow the methylene transfer reaction to the point that proton transfer becomes more favored. It has been noted that the steric bulk of a compound such as ℓ-fenchone, a ketone adjacent to two quaternary centers, can drastically slow methylene transfer. However, if these bulky ketones also have an α-hydrogen, they react cleanly with **1** to afford titanocene methyl enolates instead of the expected terminal olefin. A comparison of the characteristics of some ketones that undergo methylene transfer and similar ones that react to form enolates (Table 6) demonstrates that this dichotomy in reactivity is dictated strictly by sterics. There is no correlation with the relative acidities of the ketones. As a general rule, it appears that ketones adjacent to a quaternary center and having at least one α-hydrogen react with **1** to afford enolates.

Scheme 2 outlines a possible explanation for this reactivity using pinacolone as an example. It is presumed that there is a rapid pre-equilibrium in which the ketone coordinates to the titanocene methylidene. With less bulky ketones, the reaction would take pathway A and form an oxa-metallacycle, which would then cleave to give the terminal olefin. However, in ketones such as pinacolone, the interaction with one of the cyclopentadienyl rings precludes this intermediate. Pathway B is then more competetive. The formation of an enolate puts the *tert*-butyl group out of contact with the rings and produces a strong Ti–O bond.

This is the first evidence that the formation of the proposed oxa-metallacycle intermediate does have steric limitations. The steric limitations here roughly parallel those seen in studies on the formation and subsequent stability of titanacyclobutanes produced from the Tebbe reagent and terminal olefins.[18] However, the steric requirements for formation of the oxa-metallacycle do not appear to be as strict as those for the formation of a titanacyclobutane. This difference could be due to a number of factors. In the reaction with carbonyl compounds, there would

be a stronger coordination of the oxygen to the titanium, thus holding the ketones in the coordination sphere, readily available for reaction. Furthermore, even if this coordination equilibrium lies predominantly to the left, there is a much stronger thermodynamic driving force for the intermediate to cleave and form the final products. Cleavage of the titanacyclobutanes renders only starting material. (See Scheme 1.) For these reasons, the steric limitations are not as great, but these results show that at some point, a limit is reached, thereby making other reaction pathways more accessible.



Scheme 3. Reactions of titanocene methylidene with carbonyl carbons adjacent to a quaternary center.

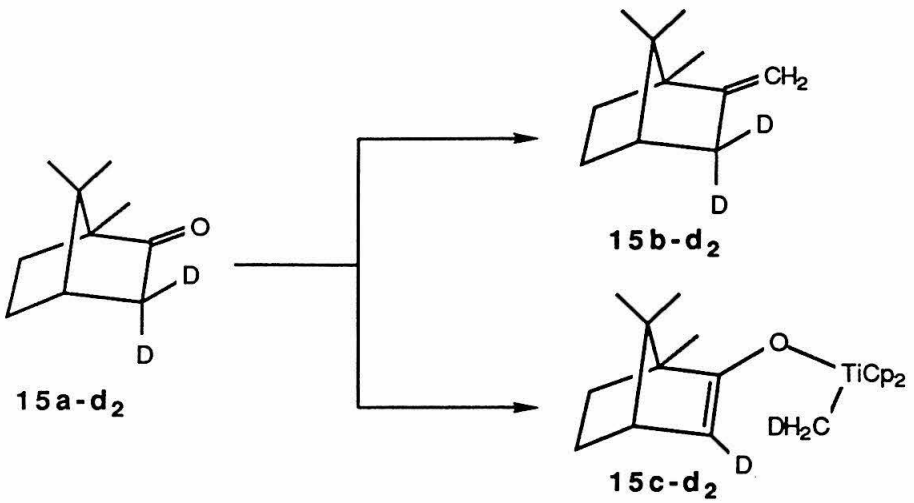
The series of compounds in Scheme 3 demonstrates the differences in reactivity of compounds having a carbonyl carbon adjacent to a quaternary center. Pivalaldehyde **29a** undergoes methylene transfer. The intermediate can avoid the severe steric interactions of the *tert*-butyl group with the cyclopentadienyl ring by puckering the oxa-metallcycle to point the β-hydrogen toward a ring and the *tert*-butyl group out and away from the rings. The corresponding β-*tert*-butyl substituted titanacyclobutane is one of the most stable of these compounds.[18] Pivaloyl chloride and pivaloyl anhydride **30a** would probably have steric problems in the intermediate, but both have good leaving groups that can rapidly β-eliminate a good leaving group and rearrange to form the less crowded enolates **30b**. Because of its steric bulk, it is unlikely that pinacolone **24a** forms the oxa-metallacycle. If it could form this intermediate, it would presumably rapidly proceed to the corresponding olefin and $[Cp_2Ti{=}O]_n$. Instead, what is observed is the abstraction of a proton by **1** to form a titanocene methyl enolate **24b**. Finally, in methyl pivaloate **31a**, in which the ester moiety is next to a quaternary center, there is no reaction seen with **1** from either **2** or **3**. Based on the fact that pivaloyl anhydride will react, assuming that there is an oxa-metallacycle formed prior to β-elimination, the results with this ester are somewhat surprising.[25] It may be that the β-elimination step with anhydrides and acid chlorides drives the reactions with these substrates. Without a good leaving group or α-hydrogen, this compound apparently has no energetically favorable pathway open to it.

Camphor is an interesting case that violates the general rule regarding enolization of ketones. Although the carbonyl carbon is adjacent to a quaternary center, the methylenation product can be isolated. However, in the original methylenation experiments, it was noted that even with an excess of titanocene methylidene, some starting material was always recovered. After the discovery of enolate production with sterically hindered ketones, it was thought that perhaps some of the

camphor was reacting with **1** to form an enolate. The enolate would then be hydrolyzed in the aqueous workup, giving the appearance of unreacted starting material. This idea prompted a reinvestigation of the reaction. Low-temperature ^{1}H NMR was used to monitor the reaction between the temperatures of −50 °C and 0 °C, but the results of this experiment were inconclusive. The cyclopentadienyl region contained several peaks, two of which at about 5.7 ppm could possibly be rationalized as being those for a camphor enolate. The upfield region of the spectrum was obscured by the signals for the methylenation product.

A more definitive experiment testing the hypothesis of partial enolization was necessary. A deuterium-labeling study furnished an unequivocal answer to this question. The α-deuterated camphor was prepared by deuterium exchange under basic conditions. If camphor were being enolized to some extent, the ^{2}H NMR spectrum should show signals for the alkene as well as distinctive signals for the enolate and the titanium-bound methyl group. (See Scheme 4.) The only signals seen in the ^{2}H NMR spectrum were two singlets for the methylenation product plus two for residual starting material. So far, this compound is the only exception to the general rule regarding enolization of sterically hindered ketones.

Camphor would appear to be a good candidate for enolization with **1** based on sterics, especially because it is also easily enolized under basic conditions; however, reaction with **1** results exclusively in methylene transfer. This result is most likely due to the unfavorable thermodynamics of the formation of a stable enolate. Although the ketone is sterically hindered, thus slowing methylene transfer and ostensibly favoring enolization, camphor is further constrained by its bicyclic system. Enolization would introduce a double bond as well as a great deal of strain into this system. Therefore, for camphor, methylene transfer *is the* preferred,



Scheme 4. Methylenation vs. enolization of camphor.

albeit slow, reaction. Because this reaction is slow, decomposition of the titanium reagent is probably competing with methylene transfer, providing unreacted starting material.

With partial enolization of camphor ruled out, it appears that all ketones tested react through only one of the two pathways outlined in Scheme 2. At no time is a mixture of products ever observed.

Reactivity of Titanocene Methyl Enolates

These methyl enolates are quite different from the chloride enolates, in both stability and physical appearance. In contrast to the titanocene chloride enolates, most of these methyl enolates are quite thermally stable. Only slight decomposition of **24b** was seen after heating to 80 °C for several hours in toluene. This decomposition was detected by the decrease in integration of the cyclopentadienyl signal in the NMR spectrum, with no new identifiable products growing in. Also, instead of being easily isolated as orange powders, the methyl enolates are red oils.

Although the oils are apparently pure by NMR, attempts at obtaining satisfactory elemental analyses were unsuccessful.

In order to determine their nucleophilicity and reactivity, these complexes were treated with alkylating agents. The pinacolone methyl enolate was treated with two equivalents of MeI for 12 h in refluxing DME. This treatement produced no detectable alkylation. Longer reaction times and other solvents such as *p*-dioxane gave the same results. The chloride enolate counterparts are also not very readily alkylated, but it is not clear whether this is due to an inherent non-nucleophilic nature or the competing decomposition that occurs under the reaction conditions.

Titanocene chloride enolates undergo aldol condensations with aldehydes between 0 °C and 25 °C to produce β-hydroxyketone products in good yield.[23,24] However, the corresponding methyl enolates do not react with aldehydes to effect aldol condensation at temperatures up to 80 °C. This result demonstrates how the exchange of a chloride for a methyl group significantly reduces the Lewis acidity of the metal center in these enolates.

In the attempts to effect aldol condensation with these enolates, another observation was made. Under these conditions, the reaction does not appear to be reversible. There was no evidence of titanocene methylidene being trapped by the potential aldol substrate.

The enolates produced by the reaction of **1** with hindered ketones do not appear to be important compounds with regard to their capacity to act as enolates. There is no potential for regioselective enolate formation, because **1** forms enolates with ketones having only a single possible enolate isomer. Also, all the reactivity studies indicate that these compounds show little or no promise in transformations generally associated with metal enolates such as aldol condensations

and alkylation. The production of titanocene methyl enolates is, however, an important discovery because it demonstrates that there are steric limitations to the methylenation of ketones using titanocene methylidene.

SUMMARY

The nucleophilic and nonbasic character of these titanium reagents is demonstrated by the lack of epimerization of α-chiral centers in reactions with optically active ketones. Because of these properties, we have been able to demonstrate that **1** cleanly converts easily enolizable ketones to terminal olefins. These alkene products are easily isolated in high yield.

The titanocene methylidene has proven to be a versatile reagent for synthesis which shows selectivity between similar functional groups. It is very selective for ketones over esters. There is also a demonstration of regioselectivity for less sterically hindered ketones.

Previous to this work, **1** had been shown to react with carbonyl-containing compounds in two distinct ways, the first of which is methylene transfer. This is the most common, occurring with aldehydes and most ketones and esters. The second pathway is enolate formation *via* β-elimination, provided that a good leaving group is present. This type of reactivity is seen with acid halides and anhydrides. Both pathways are assumed to involve an oxa-metallacycle intermediate. This work presents a third type of reactivity involving a completely different mechanism. With very sterically hindered ketones, proton transfer becomes the dominant reaction, and titanocene methyl enolates are formed. These enolates are much less Lewis acidic than those formed from acid chlorides and anhydrides and do not effect aldol condensations with aldehydes and ketones.

EXPERIMENTAL SECTION

General Considerations. All manipulations of air- and/or water-sensitive compounds were performed using standard high-vacuum or Schlenk techniques. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). Solid organometallic compounds were transferred and stored in a nitrogen-filled Vacuum Atmospheres glovebox, equipped with an MO-40-1 purification train, DK-3E Dri-Kool conditioner, and Dri-Cold freezer. Flash chromatography was performed by the procedure of Still,[28] using Woelm 32-63 (32-63 μm). Thin layer chromatography was performed on EM Reagents 0.25 mm silica gel 60-F plates and visualized with either iodine vapor or phosphomolybdic acid/ethanol spray. All reaction temperatures were measured externally.

Materials. Toluene, diethylether, and tetrahydrofuran (THF) were stirred over CaH_2, then transferred onto purple sodium-benzophenone ketyl. Pentane and hexane were stirred over concentrated H_2SO_4, washed with H_2O, dried over CaH_2, then transferred onto purple sodium-benzophenone ketyl solubilized with tetraglyme. Dichloromethane was stirred over P_2O_5 or CaH_2 and degassed by repeated freeze-pump-thaw cycles. Dried degassed solvents were vacuum-transferred into dry glass vessels equipped with Teflon valve closures and stored under argon. Benzene-d_6, toluene-d_8, and THF-d_8 (Cambridge Isotopes) were dried and vacuum-transferred from purple sodium-benzophenone ketyl. Dichloromethane-d_2 (Cambridge Isotopes and Norell, Inc.) was dried over CaH_2 and degassed by several freeze-pump-thaw cycles. Chloroform-d (Aldrich) was dried over 4 Å molecular sieves. The Tebbe reagent **2** was prepared by the published procedure.[29] Titanacyclobutanes were prepared as previously described.[18] Titanocene dichloride (Boulder Scientific) was purified by Soxhlet extraction with dichloromethane followed by crystallization. Trimethylaluminum was obtained as a *2M solution*

in toluene from Aldrich. Alumina Woelm N, activity I was obtained from ICN Biochemicals and deactivated to activity III.[29] Acetophenone was obtained from MCB. Methyl benzoate was obtained from Eastman Chemicals. All other chemicals not otherwise specified were obtained from Aldrich and used without further purification.

Instrumentation. NMR spectra were recorded on a Varian EM-390 (90 MHz, ^{1}H), JEOL FX-90Q (89.60 MHz, ^{1}H; 22.53 MHz, ^{13}C), JEOL GX-400 (399.65 MHz, ^{1}H; 100.4 MHz, ^{13}C; 61.37 MHz, ^{2}H) or Brüker WM-500 (500.13 MHz, ^{1}H). Chemical shifts are reported in δ, referenced to residual solvent signals (^{1}H: C_6D_6, δ 7.15; C_7D_8, δ 2.09; THF-d_8, δ 3.58 or 1.73; CD_2Cl_2, δ 5.32; $CDCl_3$, δ 7.24; ^{13}C: C_6D_6, δ 128.0; C_7D_8, δ 20.9; THF-d_8, δ 67.4; $CDCl_3$, δ 77.0). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), coupling constant (Hz), integration and assignment. Gas chromatography analyses were performed on a Shimadzu GC-Mini-2 equipped with an SE-30 capillary column, flame-ionization detector, and a Hewlett-Packard 3390A integrator.

General procedure for reaction of ketones with the Tebbe reagent

Method A: A solution of **2** (313 mg, 1.1 mmol) in 4 ml of THF (pre-cooled to −40 °C) was prepared under Ar. To this was added 1.0 mmol of ketone. After stirring at −40 °C for 15 min, the solution was allowed to warm to room temperature. The reaction was quenched by the addition of 300 μl of 15% aqueous NaOH. The resulting dark green solution was diluted with 50 ml of pentane, dried ($MgSO_4$), filtered through Celite and concentrated. (Isolation of the product from titanium and aluminum by-products was facilitated by allowing the diluted solution to stand overnight before filtration.) The crude product was further purified by filtration through a short column of silica gel or alumina.

Method B: This method is similar to Method A except that toluene was used as the solvent, and one equivalent of pyridine was added. Further workup and purification of products were identical to that described in Method A.

General procedure for the reaction of ketones with titanacyclobutanes

A solution of **3** (304 mg, 1.1 mmol) in 4 ml of ether (pre-cooled to 0 °C) is prepared under Ar. To this is added 1.0 mmol of ketone. The reaction mixture is allowed to warm to room temperature over 30 min and then diluted with 50 ml of pentane and filtered through Celite. Further purification is effected as described for the reaction with **2**.

General procedure for NMR tube reactions of ketones with 3a

The titanacyclobutane was loaded into a tared NMR tube. A latex septum was fitted onto the tube, and it was sealed with Parafilm. Benzene-d_6 (350-400 μl) was added to the tube *via* syringe, and the solution was frozen. Liquid substrates and internal standards were then added *via* syringe, and the solution was allowed to warm to room temperature. If necessary, the tube was centrifuged upside down to deposit the titanocene oxo-polymer in the top of the tube, thus removing it from solution prior to analysis by NMR spectroscopy.

Preparation of 1-methyl-tetralone 7a[31]

A solution of 2-tetralone (1.8 ml, mmol) and pyrrolidine (2 ml, mmol) in 40 ml of benzene was heated to reflux for 4 h in a flask fitted with a Dean-Stark trap. The solution was concentrated and redissolved in 10 ml of *p*-dioxane. To this was added 5 ml of methyl iodide followed by a 13 h reflux. Then 5 ml of H_2O and 1 ml of glacial acetic acid was added followed by 5 h. of refluxing. The reaction mixture was cooled, concentrated and taken up in ether. The ethereal solution was washed with saturated aqueous $NaHCO_3$ (3 × 25 ml), dried ($MgSO_4$), and concentrated. The product was separated from a small amount of starting material by flash

chromatography eluting with pentane/ethyl acetate (9:1). Purification yielded 1.5 g of a clear oil. ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.19 (s, 4H), 3.47 (q, J=6.3 Hz, 1H), 2.88-3.19 (m, 2H), 1.44 (d, J=6.3 Hz, 3H).

Preparation of 2-phenylcyclopentanone 12a[32]

A solution of bromobenzene (4.9 ml, 47 mmol) in 30 ml of ether was added to 1.15 g (47 mmol) of magnesium metal activated by a crystal of iodine. The solution was added at such a rate to maintain moderate reflux. After the addition was complete, the Grignard solution was cooled to 0 °C. To this was added a solution of 2-chlorocyclopentanone in 20 ml of ether. The ice bath was removed, and the reaction was stirred at room temperature for 1 h. The ether was removed to give a red, very viscous oil. This oil was dissolved in 50 ml of xylenes and heated to 155 °C for 2 h. After cooling to room temperature, the reaction mixture was poured into 200 ml of ice and 50 ml of 10% HCl. This was stirred until the ice melted and was then filtered through Celite. The layers were separated, and the aqueous layer was extracted (3×50 ml) with ether. The combined layers were washed with 10% aqueous NaOH (100 ml) and H_2O (100 ml), dried ($MgSO_4$) and concentrated. The resulting dark orange oil was Kugelrohr distilled (70 °C/ 0.1 torr) to give 3.1 g of a yellow liquid. (45%) ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.10-7.36 (m, 5H), 3.06-3.50 (m, 1H), 1.61-2.65 (m, 6H).

Preparation of diazomethane

A solution of 120 ml of 50% KOH and 400 ml of ether in an Erlenmayer flask was cooled to 0 °C. To this was slowly added 42 g of nitrosomethylurea with swirling. The addition and dissolution took approximately 1 h. The ether layer was decanted onto a layer of KOH pellets covered with ether and dried at 0 °C for 45 min.

Preparation of 3-methoxy-2-methyl-2-cyclopentenone

A solution of diazomethane (prepared as previously described) was decanted into a solution of 4.0 g of 2-methyl-1,3-cyclopentadione in 50 ml of ether until the diketone solution remained yellow. Glacial acetic acid was added dropwise until the solution cleared. The solution was washed with brine (25 ml), dried ($MgSO_4$), and concentrated. The crude product was sublimed at 50 °C/ 0.01 torr to give 3.1 g of product. ^1H NMR (90 MHz, C_6D_6): δ 3.07 (s, 3H), 1.94-2.01 (m, 2H), 1.74 (br s, 5H).

Preparation of 2-methyl-3-phenyl-2-cyclopentenone 14a

Phenyl magnesium bromide was prepared in the usual manner from 1.42 g (9 mmol) of bromobenzene and 223 mg of magnesium metal in 15 ml of ether. To this was added a solution of 1.0 g (7.9 mmol) of 3-methoxy-2-methyl-pentenone in 25 ml of THF. The reaction mixture was stirred at ambient temperature for 1.5 h, poured into 50 ml of 10% HCl, and stirred for 1 h. The layers were separated, and the aqueous layer was extracted with ether (4 × 25 ml), dried ($MgSO_4$), concentrated and Kugelrohr distilled. (70 °C/ 0.05 torr) The resulting impure oil was purified by flash chromatography eluting with pentane/ether (3:1) to give 510 mg of a light yellow oil. (37%) ^1H NMR (90 MHz, $CDCl_3$): δ 7.15-7.38 (m, 5H), 4.79 (br s, 2H), 2.43-2.79 (m, 4H), 1.83 (s, 3H).

6b: ^1H NMR (90 MHz, $CDCl_3$): δ 7.09 (s, 4H), 4.86 (s, 2H), 3.53(s, 2H), 2.86 (t, J=6.3 Hz, 2H), 2.46 (t, J=6.3 Hz, 2H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 145.4, 137.0, 136.4, 128.4, 125.9, 108.3, 37.1, 31.8, 31.2.

7b: ^1H NMR (90 MHz, $CDCl_3$): δ 6.93-7.21 (m, 4H), 4.85 (s, 2H), 3.53 (q, J=7.2 Hz, 1H), 2.26-3.02 (m, 4H), 1.40 (d, J=7.2 Hz, 3H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 146.2 137.5, 137.0, 128.0, 126.3, 109.0, 37.2, 32.3, 31.8, 27.3.

8b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.70 (s, 1H), 4.15 (s, 1H), 2.62-2.83 (m, 1H), 1.27-2.47 (m, 8H), 0.95 0.95 (s, 9H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 139.7, 100.3, 37.4, 35.2, 29.7, 28.9, 27.3, 25.2, 21.3.

9b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.23 (s, 5H), 4.71 (s, 1H), 4.10 (s, 1H), 3.13-3.41 (m, 1H), 1.30-2.62 (m, 8H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 152.8, 143.4, 128.5, 128.1, 126.1, 108.3, 50.0, 36.2, 33.8, 28.5, 26.2.

10b: ^{1}H NMR (90 MHz, C_7D_8): δ 4.68 (s, 1H), 4.23 (s, 1H), 2.21-2.38 (m, 1H), 1.23-1.98 (m, 8H), 0.97 (d, J=7.1, 3H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 144.2, 105.2, 38.2, 34.6, 29.1, 28.4, 25.1, 22.9.

11b: (mixture of isomers) ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.68 (br s), 4.52 (br s), 2.28-2.39 (m), 1.77-1.93 (m), 1.15-1.69 (m), 0.97-1.10 (overlapping doublets).

12b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.20 (s, 5H), 4.95 (s, 1H), 4.53 (s, 1H), 3.26-3.79 (m, 1H), 1.44-2.65 (m, 6H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 156.4, 144.9, 128.7, 128.2, 125.9, 107.2, 51.3, 36.5, 33.4, 24.7.

13b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.25 (s, 5H), 4.87 (s, 2H), 3.17-3.42 (m, 1H), 2.85 (d, J=6.5 Hz, 2H), 1.80-2.47 (m, 4H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 154.2, 142.8, 128.3, 128.0, 126.3, 108.3, 54.2, 37.2, 34.0, 23.9.

14b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.15-7.38 (m, 5H), 4.79 (br s, 2H), 2.43-2.79 (m, 2H), 2.40-2.64 (m, 4H), 1.83 (s, 3H).

15b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.57-4.80 (m, 2H), 1.10-2.63 (m, 7H), 0.90 (d, J=2.9 Hz, 6H), 0.76 (s, 3H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 159.5, 101.0, 51.5, 47.2, 44.7, 37.0, 35.1, 28.0, 19.6, 19.0, 12.5.

15a-d_2: ^{2}H NMR (61.37 MHz, C_7H_8): δ 2.02 (br s), 1.50 (br s).

15b-d_2: ^{2}H NMR (61.37 MHz, C_7H_8): δ 2.25 (br s), 1.77 (br s).

Selectivity Competition Experiments

- **Carbonyl substrates with 2 and 3 under standard reaction conditions**

Stock solutions, equimolar in both carbonyl substrates, (listed with product ratios in Tables 2-5) were prepared in toluene. Stock solutions of **2** and **3** were prepared in toluene and benzene, respectively, immediately before the experiments were conducted. The solution of **3** was frozen while not in use. The reaction conditions were identical to those described earlier (Method B for **2**). The product ratio was determined by capillary gas chromatography analysis. Retention times and molar response ratios were determined with pure starting materials and independently prepared products.

- **Carbonyl substrates and 2 with modified reaction conditions**

Stock solutions of reactants were used as above. The conditions were modified by the addition of pyridine to a solution of carbonyl substrates cooled to −40 °C followed by the very slow addition of a toluene solution of **2**. The workup and product ratio analysis proceeded as described above.

Preparation of methyl pivaloate 31a

A solution of methanol (500 μl, 12.5 mmol) and pyridine (1.0 ml, 12.5 mmol) in 50 ml of ether was prepared and heated to reflux. This was followed by the dropwise addition of neat pivaloyl chloride (1.0 g, 8.3 mmol) to the refluxing solution. When the addition was complete, the oil bath was removed, and the reaction mixture was allowed to stir at ambient temperature for 4 h. The reaction mixture was cooled to 0 °C and filtered to remove the pyridinium hydrochloride precipitate. The resulting ethereal solution was washed with dilute HCl (20 ml) and H_2O (20 ml), dried ($MgSO_4$), and concentrated to yield a clear oil that was pure by NMR and used without further purification. ^{1}H NMR (90 MHz, C_6D_6): δ 3.32 (s, 3H), 1.10 (s, 9H).

Preparation of 1,1-dimethyl-2-tetralone 26a

Lithium diisopropyl amide was generated at −78 °C by adding 11.7 ml of 1.2M n-BuLi in hexane to 2 ml of dry diisopropyl amine in 25 ml of THF. This mixture was allowed to stir at −78 °C for 45 min. To this was added a solution of 2-tetralone (0.90 ml, 1.0 g, 6.85 mmol) in 10 ml of THF. After 30 min at −78 °C, MeI (1.7 ml, 3.8 g, 28 mmol) was added. The solution was allowed to warm to room temperature over a period of 2 h and then was quenched with 10% HCl. The layers were separated, and the aqueous layer was extracted with ether (3 × 25 ml). The combined ethereal portions were washed with brine, dried ($MgSO_4$), filtered and concentrated. The desired product was isolated from starting material and the mono-methylated product by flash chromatography eluting with pentane/ether (3:1) to yield 600 mg. (50%) ^{1}H NMR (90 MHz, $CDCl_3$): δ 6.98-7.20 (m, 4H), 3.09 (t, J=7.2 Hz, 2H), 1.43 (s, 6H).

General procedure for preparation of titanocene methyl enolates

To a solution of 1.1 equivalent of **3** in ether at 0 °C was added 1.0 equivalent of ketone. After 5-10 min, the reaction mixture was allowed to warm to room temperature. Removal of solvent *in vacuo* yielded a spectroscopically pure red oil. All attempts at crystallization were unsuccessful.

24b: ^{1}H NMR (90 MHz, C_6D_6): δ 5.70 (s, 10H), 3.86 (s, 1H), 3.35 (s, 1H), 1.01 (s, 9H), 0.86 (s, 3H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 179.2, 112.5, 81.3, 37.3, 36.2, 28.6.

26b: ^{1}H NMR (90 MHz, C_6D_6): δ 5.70 (s, 10H), 4.22 (t, J=4.3 Hz, 1H), 3.55 4.3 Hz, 2H), 1.31 (s, 6H), 0.91 (s, 3H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 167.4, 133.4, 129.0, 126.9, 125.6, 112.5, 93.5, 40.0, 36.1, 30.5, 29.1.

27b: ^{1}H NMR (90 MHz, C_6D_6): δ 5.69 (s, 10H), 4.08 (t, J=4.5 Hz, 1H), 2.00-2.34 (m, 2H), 0.97 (s, 6H), 0.86 (s, 3H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 170.3, 112.3, 96.9, 39.8, 36.5, 35.2, 27.6, 25.8, 20.5.

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16. In some instances, the dimethylated product has been seen when there was no excess of titanocene methylidene. This would imply that metallacycle formation is faster than or at least competetive with methylenation, although this is counterintuitive.

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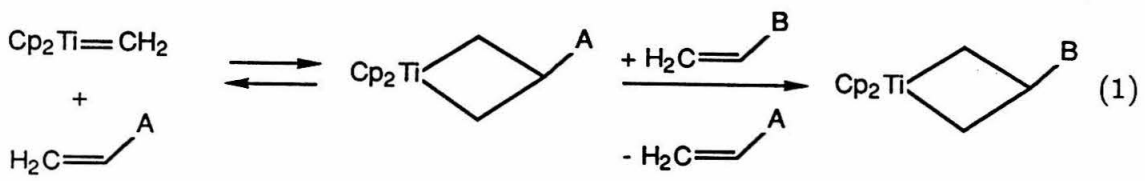
Chapter 2

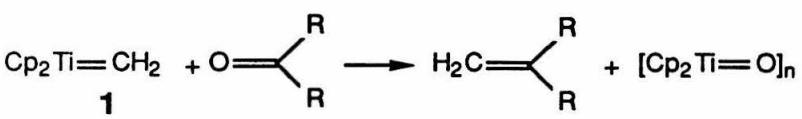
The Geminal Dimethylation of Ketones

INTRODUCTION

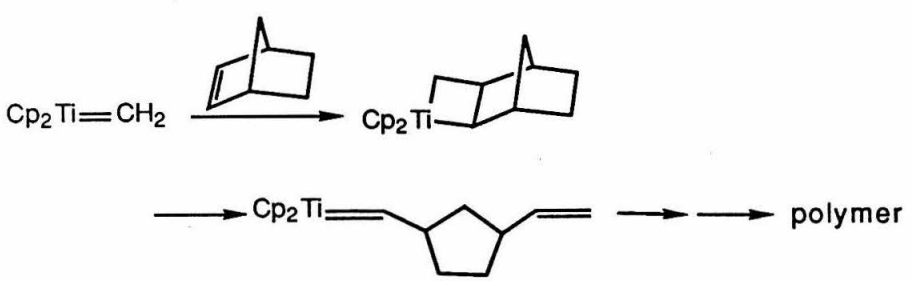
The development of uses for the reactive fragment, titanocene methylidene **1**, (and titanocene alkylidenes) has been an ongoing research interest of our group.[1,2] Some of the most important uses of **1** include catalysis of olefin metathesis[3] (see Equation 1), stoichiometric methylenation of carbonyl groups[2] (see Equation 2), and most recently, ring opening metathesis polymerization[4] (ROMP). (See Equation 3.) The fact that **1** will react with both carbonyl and olefin functionalities makes it a very versatile reagent. Although each of these different types of reactivity is important in its own right, the utility of **1** is further enhanced when the two reactions are combined.



(1)

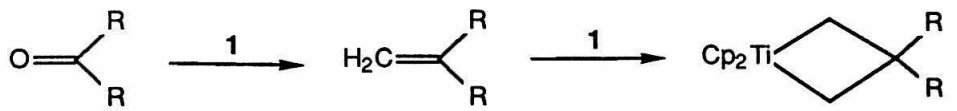


(2)



(3)

Examples of this "tandem" use of titanocene methylidene are seen in the use of a ketone to end-cap a ROMP product[4] and in an efficient synthesis of (±)-$\Delta^{(9,12)}$-capnellene.[5] Both of these examples involve productive metathesis, followed by a reaction of the thus formed titanocene alkylidene with a carbonyl group. In these examples, the substrates, alkene and carbonyl, come from two different sources.

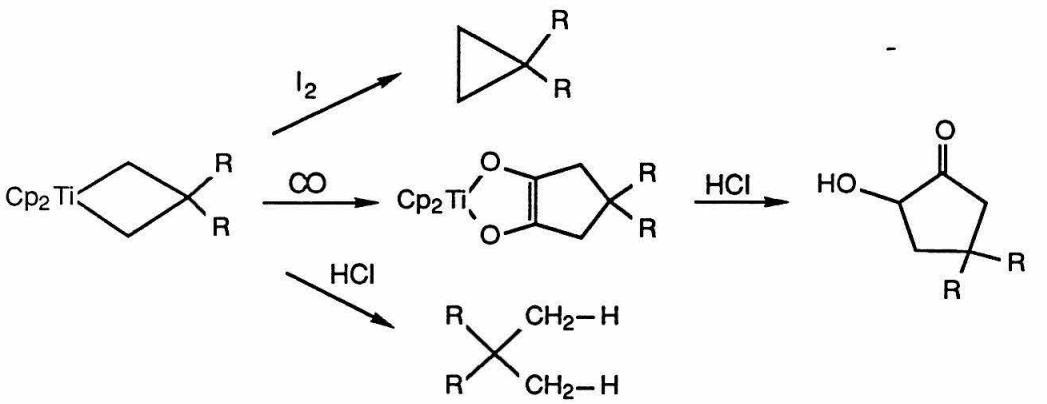


(4)

2

Another approach to combining the different reactivities is the treatment of a carbonyl-containing substrate such as a ketone with two equivalents of the particular source of **1**, either the Tebbe reagent or a titanacyclobutane. (See Equation 4.) The first equivalent of **1** reacts with the ketone to produce a terminal alkene *via* a Wittig-type methylenation. The resulting alkene is a substrate for the second equivalent of **1** and can react to produce a new β,β-disubstituted titanacyclobutane **2**. The metallacycle produced can react further in a number of different ways. Earlier studies with metallacycles have demonstrated their reactivity with various reagents.[2a] Some of these transformations include carbonylation,[6] the reductive elimination of cyclopropanes induced by photolysis[7] or oxidizing agents,[8] and cleavage of the Ti–C bonds by electrophiles.[2a] (See Scheme 1.)

Synthetically, conversion of a ketone to a β,β-disubstituted metallacycle provides a means of producing a further functionalized quaternary center. This transformation is significant in that there are many procedures for the formation of carbon-carbon bonds, but the majority of them are not applicable to the creation of a quaternary carbon. The generation of such centers is one of the most restricted processes in organic synthesis.[9]



Scheme 1. Reactions of metallacycles producing quaternary carbon centers.

The combination of these types of reactivity has been used successfully in earlier studies in the development of titanocene methylidene as a useful reagent for organic synthesis. Combining these reactions results in a wide range of one-pot annelation procedures for ketones. In fact, one cyclic acyloin synthesis has been carried out in overall 54% yield.[6] This yield after minimum optimization suggests these reactions could provide extremely efficient routes to complex systems. One-pot conversion of a ketone to a cyclopropane has also been observed.[8]

Earlier mechanistic work on metallacycles that were isolated in olefin metathesis studies indicated that electrophiles will cleave the Ti–C bonds. This produces an alkane with a geminal dimethyl center. Again, combining the two types of reactivity seen with titanocene methylidene, it appeared that we could develop a synthetic route allowing the simple and direct conversion of a ketone to a geminal dimethyl moiety.

Probably the most widely used strategy for geminal dimethylation of ketones

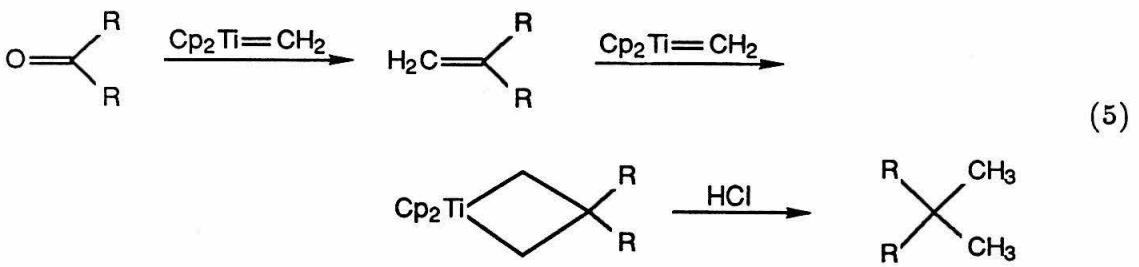
is a multistep procedure, including Wittig methylenation, Simmons–Smith cyclopropanation and hydrogenolysis.[10] Previously, it had been shown that certain ketones are geminal-dimethylated with a fourfold excess of $AlMe_3$ under pyrolysis conditions.[11] However, this method suffers from low yields because of competing enolization and rearrangement. More recent reports by Reetz[12,13] demonstrate a method allowing exhaustive methylation of ketones, using two equivalents of Me_2TiCl_2 at or below room temperature.

The development of a procedure to convert a ketone to a geminal dimethyl center under mild conditions would be a useful one. These centers appear frequently in natural products such as terpenes and steroids, and other compounds of synthetic and theoretical interest.

RESULTS AND DISCUSSION

Geminal Dimethylation Reaction

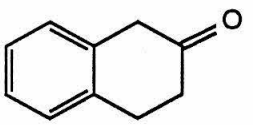
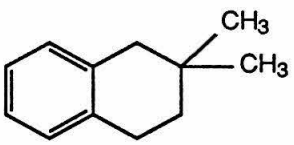
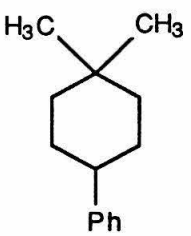
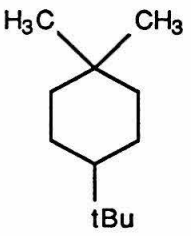
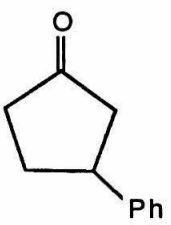
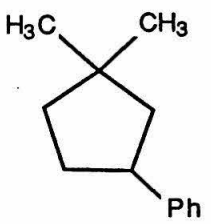
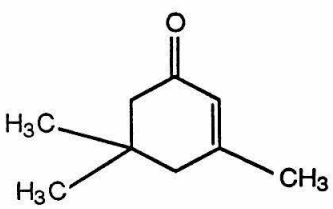
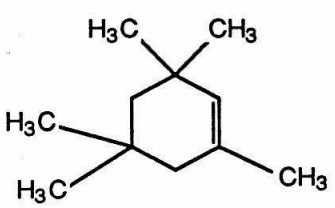
The treatment of a ketone (within certain steric limitations, which will be discussed below), with two equivalents of titanocene methylidene allows for the coupling of Wittig-type methylenation with metallacycle formation. The substrate ketone reacts with one equivalent of **1** to produce a terminal olefin. The product of this reaction is also a substrate and can react further with the second equivalent of **1** to form a new metallacycle. Protonolysis of the new metallacycle completes the process—the formal replacement of the carbonyl oxygen by two methyl groups. (See Equation 5.)



(5)

This fast, one-pot series of steps occurs under very mild conditions. This work was done using the Tebbe reagent as the source of **1**. The ketone is added to a −40 °C solution of two equivalents of the Tebbe reagent in THF. The reaction mixture is allowed to warm to −20 °C over 30 min. Protonolysis is effected by cooling the reaction mixture to −70 °C and treating it with an excess of HCl gas. After protonolysis, the reaction mixture is allowed to warm to room temperature and is diluted with pentane, or pentane and ether. The titanium and aluminum by-products are easily removed by filtration through a short column of Celite and silica gel in a Büchner funnel. Concentration of the eluant allows for isolation of a

Table 1. Ketone substrates and their dimethylated products

ketone	product	yield
 **3a**	 **3b**	85
 **4a**	 **4b**	87
 **5a**	 **5b**	89
 **6a**	 **6b**	68
 **7a**	 **7b**	79

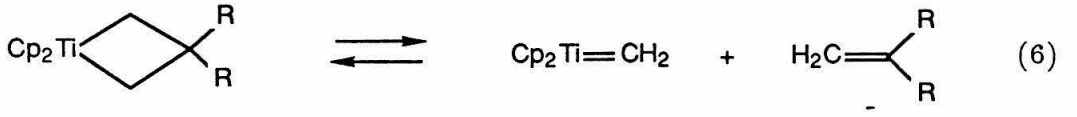
product of generally high purity. Isolation of the dimethylated product from any alkene formed from incomplete reaction can be achieved by flash chromatography.

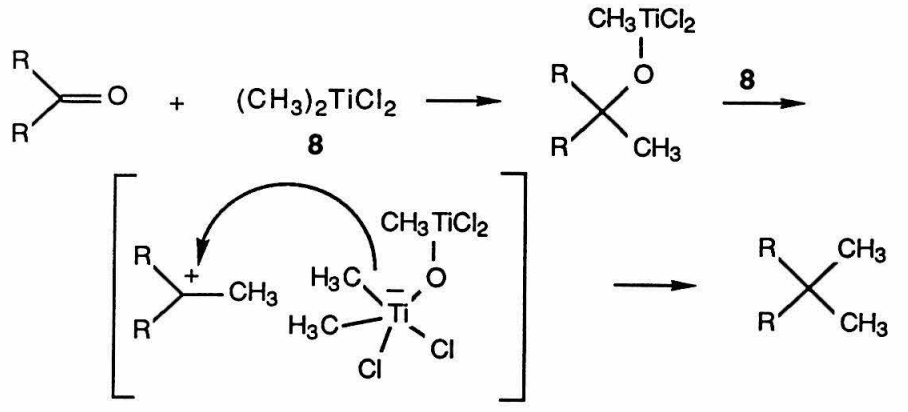
The utility of this procedure is illustrated by the ketone substrates and their geminal dimethylated products listed in Table 1. The products in these reactions are formed and isolated in moderate-to-high yield. It appears that lightly substituted cyclic ketones are good candidates for this direct geminal dimethylation procedure, presumably because the alkenes formed from methylenation of these ketones form very stable metallacycles. Earlier work[14] on the stability of metallacycles have shown these β-spiro-metallacycles to be quite stable.

The high stability of such metallacycles was also noted in some of our methylenation work.[2c,15] It was observed that metallacycle formation with 2-tetralone was so facile and the metallacycle so stable that it was difficult to simply methylenate this compound without obtaining some of the dimethylated product under standard reaction conditions. The fact that some of the dimethylated product was being produced indicated that protonolysis of the metallacycle could be effected under the basic conditions used in the workup of the methylenation reaction. With an excess of **1**,[16] the alkene product reacts to form a metallacycle that undergoes protonolysis in the workup with 15% NaOH at -20 °C.

For dimethylation, this basic workup appears to be inferior to treatment with HCl gas at -70 °C. At this lower temperature, the metallacycles are more stable, and protonolysis is very fast. Protonolysis with an aqueous base is slower. The equilibrium of metallacycle cleavage (see Equation 6) lies farther to the right at the higher temperature at which the basic workup is done, giving a lower ratio of dimethyl-to-alkene products.

Another procedure for the conversion of ketones to geminal dimethyl centers is that reported by Reetz.[13] This method uses Me_2TiCl_2 **8** to effect this transformation. (See Scheme 2.) His proposed mechanism involves the addition of Ti–CH_3

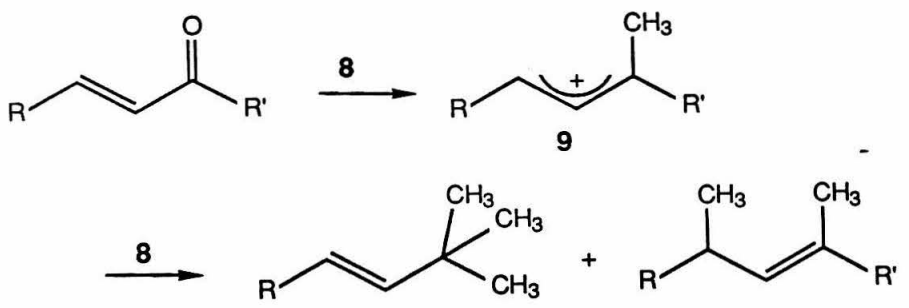




Scheme 2. Reetz' procedure and proposed mechanism for geminal dimethylation using $(CH_3)_2TiCl_2$.

across the C=O bond. The carbocation that is subsequently formed reacts with a second equivalent of **8** to afford the dimethylated product. Although this method has not yet seen widespread use, it does show promise for use with many types of ketones. One restriction on this method involves α,β-unsaturated ketones. In an attempt to apply this procedure to this type of substrate, products were obtained that imply the intermediacy of an ambident allyl cation **9**. (See Equation 7.) On the other hand, the results in Table 1 show that titanocene methylidene works quite well with α,β-unsaturated ketones. There is no problem of additional products from cation rearrangements as observed in the Reetz procedure, since the reaction with **1** goes through an entirely different mechanism,

This method has some great advantages over the older methodologies used to effect geminal dimethylation of ketones. Simply in terms of mildness of reaction



(7)

conditions, this procedure is superior to the older procedure of using $AlMe_3$ under pyrolysis conditions. The use of **1** is also an advancement over the multistep approach involving methylenation, cyclopropanation and hydrogenolysis. Although the reaction using **1** also appears to be three separate reactions, it is actually a fast, one-pot operation. The former process is a much more complex series of separate and more labor-intensive reactions.

Another problem with the older method lies in the first step, the Wittig methylenation. Because the phosphorus ylides used in this reaction are quite basic, enolization becomes the dominant reaction with easily enolizable ketones; proton transfer is rapid relative to methylenation. On that basis, the use of this methodology is precluded for ketones of this type. On the other hand, these ketones are quite readily methylenated with titanocene methylidene. This reagent is nonbasic relative to the rate of methylene transfer.[18]

Steric Limitations of Metallacycle Formation

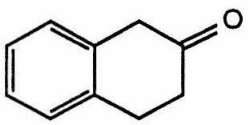
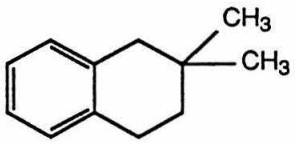
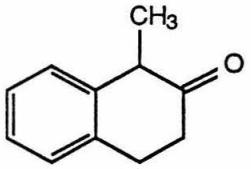
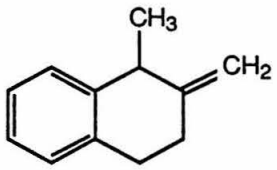
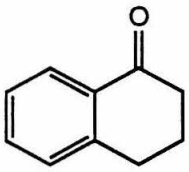
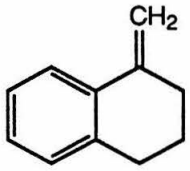
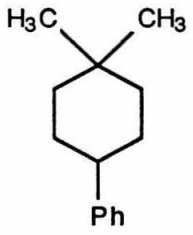
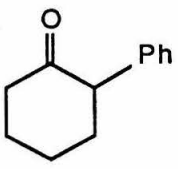
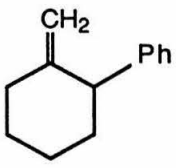
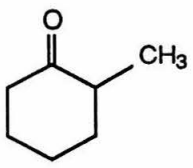
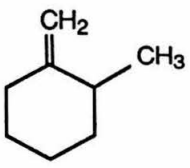
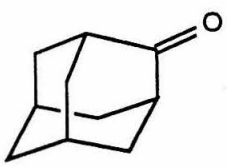
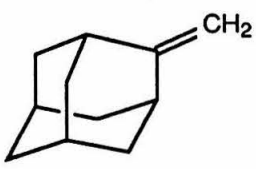
An examination of the ketones in Table 1 indicates that compounds that are good substrates are ones that are relatively unsubstituted. Indeed, a restriction on this procedure is that the carbonyl in the ketone substrate must be adjacent to two methylene groups. A comparison of these ketones shown to be good candidates with those listed in Table 2 confirms this. It appears that a single substituent on the α-carbon can block the formation of the desired geminal dimethyl product.

Subjecting these α-substituted ketones[18] to the general geminal dimethylation procedure produces only an alkene product—that formed from methylenation, identical to the alkene produced by treatment with a single equivalent of titanocene methylidene. The second equivalent of **1** remains unreacted. Therefore, the difficulty apparently lies either in the formation of a metallacycle from the alkene product or in the protonolysis thereof.

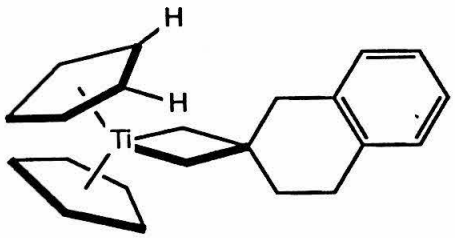
There is no obvious reason why protonolysis should be significantly more difficult for a given metallacycle over another. All terminal alkenes form similar β,β-disubstituted metallacycles. Therefore, the environment at the metal center, the site where protonolysis occurs, should not vary greatly with different substrates. In light of the earlier studies on the stability of metallacycles, either the possibility of a problem with the formation of a metallacycle or its instability under the reaction conditions seemed to be more likely causes of incomplete reaction. To test this hypothesis, the reaction was monitored using low-temperature ^{1}H NMR spectroscopy. Presumably, this would allow direct observation of a metallacycle. The thought was that α-substituted ketones might require modified reaction conditions such as lower temperatures. Variable-temperature NMR would allow the determination of a temperature at which the metallacycle would be formed and could undergo protonolysis. The low-temperature NMR experiments were performed in toluene-d_8 with the addition of two equivalents of pyridine to effect dissociation of dimethylaluminum chloride.

The first ketone monitored was 2-tetralone, a ketone that *does* undergo facile geminal dimethylation. Product analysis gives independent evidence that a metallacycle is formed with the methylenation product of this ketone. Monitoring the reaction of **1** with 2-tetralone first provides a check on the experiment. It establishes that under the experimental conditions, metallacycle formation that is presumed to occur can, in fact, be observed spectroscopically. Other substrates

Table 2. Ketone substrates and their products

ketone		product	
	**3 a**		**3 b**
	**11 a**		**11 b**
	**12 a**		**12 b**
	**4 a**		**4 b**
	**13 a**		**13 b**
	**14 a**		**14 b**
	**15 a**		**15 b**

could be compared accordingly. The results of the experiment using 2-tetralone were very straightforward. The methylenation reaction was very fast at −40 °C as evidenced by NMR signals for the new alkene. This was followed by metallacycle formation. The progression of the second reaction could be observed by new signals for the newly formed metallacycle, particularly the cyclopentadienyl rings just upfield from the signal for the Tebbe reagent and the AB quartet for the α-protons. These signals grow in at the the expense of those for the alkene produced in the first step; this can be seen clearly in the spectrum shown in Figure 1. This spiro-metallacycle **10** produced from the methylenation product of 2-tetralone is formed at −40 °C and is stable up to room temperature.



10

Similar low-temperature NMR experiments were repeated on other substrates for which geminal dimethylation had not been previously observed. As a direct comparison with 2-tetralone, 1-methyl-2-tetralone was used as a substrate. Again, methylenation occurred quite rapidly. However, at temperatures ranging from −70 °C to +20 °C, the equilibrium for any metallacycle formation that might be occurring lies too far to the left for it to be observed. The signals for the olefinic protons never disappeared, as would be the case with the production of a new metallacycle. Other ketones examined in this type of experiment, which gave the same negative results, were 1-tetralone **12a**, 2-phenylcyclohexanone **13a**, and adamatanone **15a**. The fact that 1-methyleneadamantane does not form a

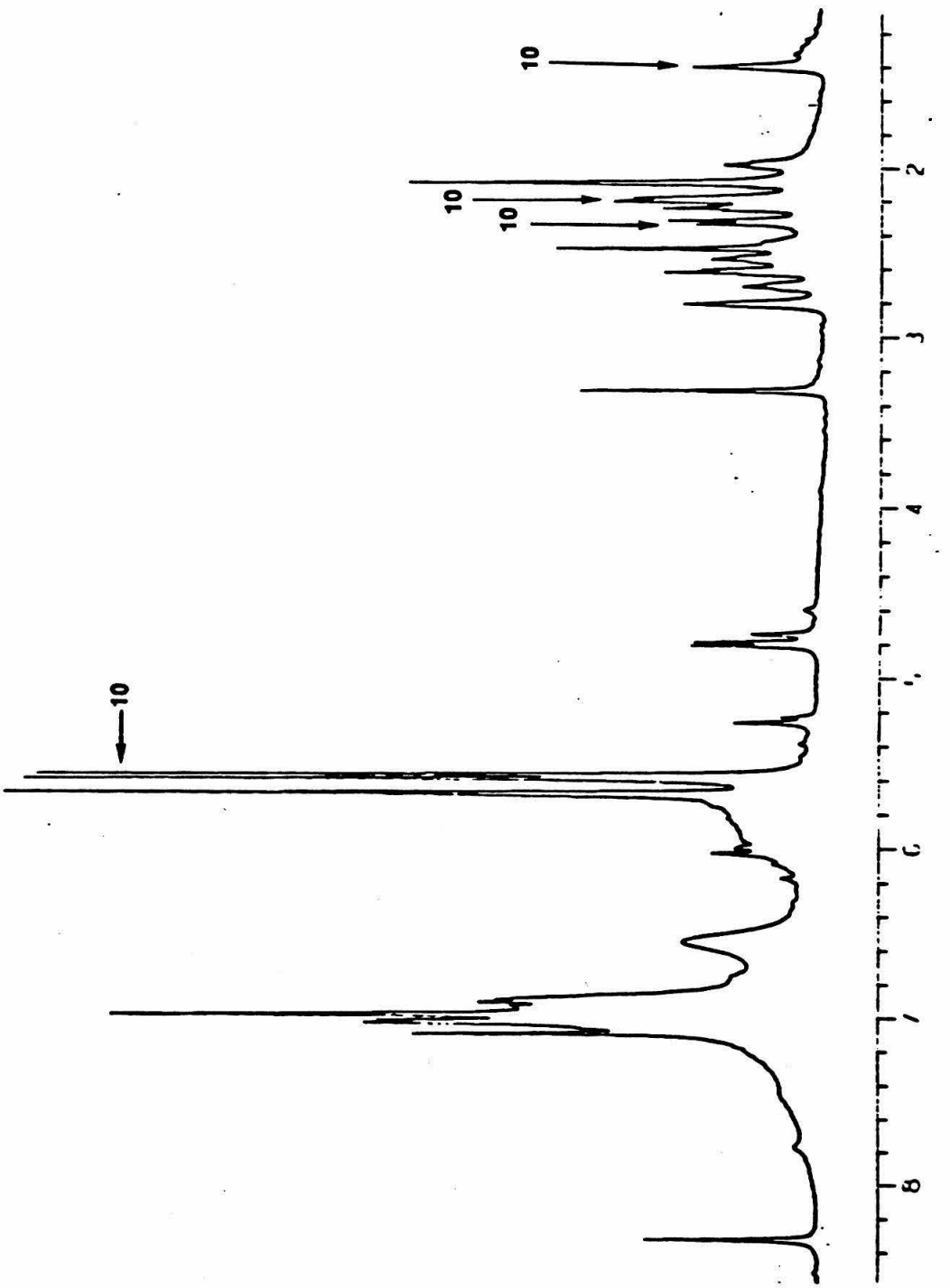
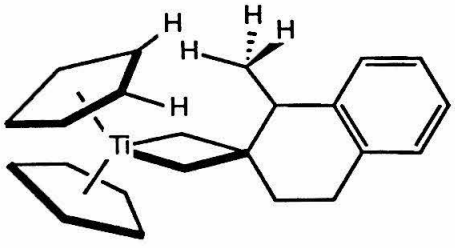
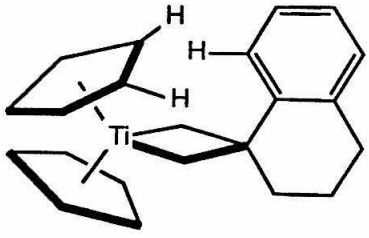


Figure 1. 400 MHz NMR spectrum showing metallacycle **10** and the alkene produced from methylenation of 2-tetralone.

metallacycle was somewhat surprising. It was thought that the substituents should be more constrained by the ring structure, thereby decreasing steric interactions with the cyclopentadienyl rings. This, however, did not appear to be the case. These results imply significant steric interactions between any α-substituents and the cyclopentadienyl rings in the metallacycle, if it were to be formed.





SUMMARY

Titanocene methylidene reacts with carbonyl moieties as well as alkenes. Through the combination of these two types of reactivity, we have developed a simple, one-pot method for creating a geminal dimethyl center from a ketone. In examining the scope of this reaction, we have found that it is a sterically restricted process in that only ketones with no α-substituents will undergo this transformation. However, it is a mild method, complementary to Reetz's procedure, in which a more highly substituted ketone is the favored substrate. It also gives only one product with α,β-unsaturated ketones, whereas Reetz's procedure gives a mixture. This reaction is yet another way in which titanocene methylidene can be used to convert a ketone to a quaternary center.

EXPERIMENTAL SECTION

General Considerations. All manipulations of air- and/or water-sensitive compounds were performed using standard high-vacuum or Schlenk techniques. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). Solid compounds were transferred and stored in a nitrogen-filled Vacuum Atmospheres glovebox, equipped with an MO-40-1 purification train, DK-3E Dri-Kool conditioner, and Dri-Cold freezer. Flash chromatography was performed by the procedure of Still,[20] using Woelm 32-63 (32-63 μm). Thin-layer chromatography was performed on EM Reagents 0.25 mm silica gel 60-F plates and visualized with either iodine vapor or phosphomolybdic acid/ethanol spray. All reaction temperatures were measured externally.

Materials. Toluene, diethylether, and tetrahydrofuran were stirred over CaH_2, then transferred to purple sodium-benzophenone ketyl. Pentane and hexane were stirred over concentrated H_2SO_4, washed with H_2O, dried over CaH_2, then transferred to purple sodium-benzophenone ketyl solubilized with tetraglyme. Dichloromethane was stirred over P_2O_5 or CaH_2 and degassed by evacuation of freeze-pump-thaw cycles. Dried degassed solvents were vacuum-transferred into dry glass vessels equipped with Teflon valve closures and stored under argon. Benzene-d_6, toluene-d_8, and tetrahydrofuran-d_8 (Cambridge Isotopes) were dried and vacuum-transferred from purple sodium-benzophenone ketyl. Chloroform-d (Aldrich) was dried over 4 Å molecular sieves. Dichloromethane-d_2 (Cambridge Isotopes and Norell, Inc.) was dried over CaH_2 and degassed by several freeze-pump-thaw cycles. The Tebbe reagent was prepared as previously described.[21] Titanocene dichloride (Boulder Scientific) was purified by Soxhlet extraction with dichloromethane, followed by crystallization. Trimethylaluminum was obtained from Aldrich. 1-Methyl-2-tetralone was prepared as described in Chapter 1 of this

thesis. All other chemicals not otherwise specified were obtained from Aldrich and used without further purification.

Instrumentation. NMR spectra were recorded on a Varian EM-390 (90 MHz, ^{1}H), JEOL FX-90Q (89.60 MHz, ^{1}H; 22.53 MHz, ^{13}C), JEOL GX-400 (399.65 MHz, ^{1}H; 100.4 MHz, ^{13}C) or Brüker WM-500 (500.13 MHz,^{1}H). Chemical shifts are reported in δ, referenced to residual solvent signals (^{1}H: C_6D_6, δ 7.15; C_7D_8, δ 2.09; THF-d_8, δ 3.58 or 1.73; CD_2Cl_2, δ 5.32; $CDCl_3$, δ 7.24; ^{13}C: C_6D_6, δ 128.0; C_7D_8, δ 20.9; THF-d_8, δ 67.4; $CDCl_3$, δ 77.0).Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), coupling constant (Hz), integration and assignment. Gas chromatography analyses were performed on a Shimadzu GC-Mini-2 equipped with an SE-30 capillary column, flame-ionization detector, and a Hewlett-Packard 3390A integrator.

General procedure for the dimethylation of ketones.

A solution of 455 mg (1.6 mmol) of the Tebbe reagent in 5 ml of THF (precooled to −40 °C) was prepared. To this was added 0.7 mmol of the ketone substate. Liquid substrates were added neat through a rubber septum, *via* syringe. Solid substrates were added against a stream of argon. The reaction mixture was allowed to stir at −40 °C for 15-30 min. Then the solution was warmed to −20 °C over 90 min.

HCl workup: The reaction mixture was cooled to −78 °C and treated with an excess of anhydrous HCl *via* syringe. This was allowed to stir at −78 °C for a few minutes then gradually warm to room temperature. The room temperature mixture was diluted with pentane to precipitate titanium and aluminum by-products. The solution was filtered through a short column of silica gel, eluting with pentane and a small amount of ether.

NaOH workup: To the −20 °C reaction mixture was added 300 μl of 15% aqueous NaOH. The solution was stirred and allowed to warm to room temperature. The titanium and aluminum by-products were precipitated by the addition of pentane, and the rest of the workup and purification proceeded as described above in the HCl workup.

3b ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.07 (s, 4H), 2.80 (t, J=7.2 Hz, 2H), 2.53 (s, 2H), 1.55 (t, J=7.2 Hz, 2H), 0.98 (s, 6H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 136.4, 135.7, 129.5, 128.7, 125.4, 43.5, 35.9, 29.4, 28.1, 26.5, 22.6.

4b ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.23 (s, 5H), 2.21-2.63 (m, 8H), 1.05-1.79 (m, 1H), 0.99 (s, 3H), 0.94 (s. 3H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 147.8 128.3 126.8, 125.8, 44.6, 39.8, 33.2, 30.2, 29.8, 24.3.

6b ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.23 (s, 5H), 3.00-3.39 (m, 1H), 1.34-2.40 (m, 6H), 1.13 (s, 3H), 1.07 (s, 3H).

7b ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.23 (s, 1H), 1.67 (s, 3H), 1.56 (s, 2H), 1.16 (s, 2H), 0.94 (s, 12H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 131.7, 126.5, 43.6, 43.1, 35.5, 31.0, 27.9, 24.7, 22.5.

11b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 6.93-7.21 (m, 4H), 4.85 (s, 2H), 3.53 (q, J=7.2 Hz, 1H), 2.26-3.02 (m, 4H), 1.40 (d, J=7.2 Hz, 3H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 146.2 137.5, 137.0, 128.0, 126.3, 109.0, 37.2, 32.3, 31.8, 27.3.

12b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 6.99-7.80 (m, 4H), 5.45 (d, J=1.2 Hz, 1H), 4.92 (d, J=1.2 Hz, 1H), 2.82 (t, J=7.8 Hz, 2H), 2.54 (t, J=7.8 Hz, 2H), 1.69-2.03 (m, 2H).

13b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 7.23 (s, 5H), 4.71 (s, 1H), 4.10 (s, 1H), 3.13-3.41 (m, 1H), 1.30-2.62 (m, 8H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 152.8, 143.4, 128.5, 128.1, 126.1, 108.3, 50.0, 36.2, 33.8, 28.5, 26.2.

14b: ^{1}H NMR (90 MHz, C_7D_8): δ 4.68 (s, 1H), 4.23 (s, 1H), 2.21-2.38 (m, 1H), 1.23-1.98 (m, 8H), 0.97 (d, J=7.1, 3H); ^{13}C NMR (22.53 MHz, $CDCl_3$): δ 144.2, 105.2, 38.2, 34.6, 29.1, 28.4, 25.1, 22.9.

15b: ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.50 (s, 2H), 2.48 (bs, 4H), 1.84 (d, J=1.8 Hz, 8H).

REFERENCES AND NOTES

1. The isolable reagents used as sources of titanocene methylidene in this work are discussed in Chapter 1 of this thesis.

2. For some examples see: (a) Brown, K. A.; Buchwald, S. L.; Cannizzo, L. F.; Clawson, L.; Ho, S.; Meinhart, J. D.; Stille, J. R.; Straus, D. A.; Grubbs, R. H. *Pure Appl. Chem.*, **1983**, *55*, 1733. (b) Pine, S. H.; Zahler, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.*, **1980**, *102*, 3270. (c) Clawson, L.; Buchwald, S. L.; Grubbs, R. H. *Tetrahedron Lett.*, **1984**, 5733.

3. Tebbe, F. N.; Parshall, G. W.; Reddy, G. S.; *J. Am. Chem. Soc.*, **1978**, *100*, 3611. (b) Lee, J. B.; Ott, K. C.; Grubbs, R. H. *J. Am. Chem. Soc.*, **1982**, *104*, 7491, and references therein. (c) Grubbs, R. H. *Prog. Inorg. Chem.*, **1978**, *104*, 7491.

4. Gilliom, L. R.; Grubbs, R. H. *J. Am. Chem. Soc.*, **1986**, *108*, 1733.

5. Stille, J. R.; Grubbs, R. H. *J. Am. Chem. Soc.*, **1986**, *108*, 855.

6. Straus, D. A., Ph.D. Thesis, California Institute of Technology, 1983.

7. Tumas, W.; Wheeler, D. R.; Grubbs, R. H. *J. Am. Chem. Soc.*, **1987**, *109*, 6182.

8. Ho, S. C. H., Ph.D. Thesis, California Institute of Technology, 1986.

9. Martin, S. F. *Tetrahedron*, **1980**, *36*, 419.

10. (a) Groger, C.; Musson, H.; Rossnage, I. *Chem. Ber.*, **1980**, *13*, 3621. (b) Oppolzer, W.; Godel, T. *J. Am. Chem. Soc.*, **1978**, *100*, 2583.

11. Meisters, A.; Mole, T. *Aust. J. Chem.*, **1974**, *27*, 1665.

12. For extensive examples and refence listings, see: Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Spring-Verlag: Berlin, **1986.**

13. (a) Reetz, M. T.; Westermann, J.; Steinbach, R. *J. Chem. Soc., Chem. Commun.*, **1981**, 237. (b) Reetz, M. T.; Westermann, J.; Kyung, S. H. *Chem. Ber.*, **1985**, *118*, 1050.

14. Straus, D. A.; Grubbs, R. H. *Organometallics*, **1982**, *1*, 1658.

15. Chapter 1 of this thesis.

16. Even when no excess of titanocene methylidene is used in the reaction with 2-tetralone, some of the dimethylated product as well as some unreacted starting material is observed. This result has also been observed by other workers.[17]

17. Pine, S. H.; Pettit, R. J.: Geib, G. D.; Cruz, S. G.; Gallego, C. H.; Tijerina, T.; Pine, R. D. *J. Org. Chem.*, **1985**, *50*, 1212.

18. We have seen that very enolizable ketones are readily methylenated without any sign of competing enolization.[15]

19. For purposes of this discussion, a ketone with no α-substituents is defined as one in which the carbonyl group is adjacent to two methylene groups.

20. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.*, **1978**, *43*, 2923.

21. Lee, J. B.; Ott, K. C.; Grubbs, R. H. *J. Am. Chem. Soc.*, **1982**, *104*, 7491.

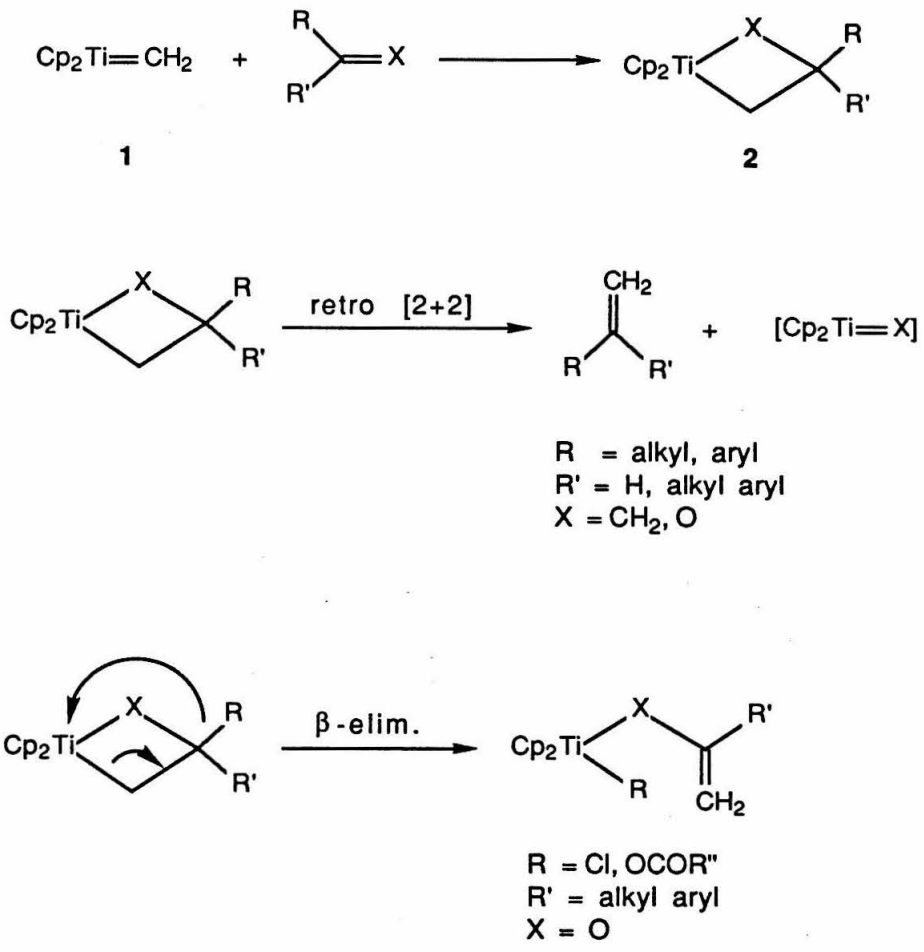
Chapter 3

The Reactivity of Titanocene Methylidene with Imines and Heterocycles Containing a C=N Bond

INTRODUCTION

The reactivity of titanocene methylidene **1** (generated from either a substituted titanacyclobutane or Tebbe's reagent[1]) has been examined with a number of unsaturated organic substrates.[2] It has been observed that **1** will undergo [2 + 2] cycloadditions with C=X multiple bonds (X=C, O), generating cyclic intermediates **2** that subsequently decompose to form products *via* two distinct reaction pathways as shown in Scheme 1. For example, alkenes react to produce a new metallacycle and release another alkene. This process is olefin metathesis. With carbonyl-containing compounds, the intermediate formed is an oxa-metallacycle. With ketones, aldehydes and esters, this intermediate cleaves to give a methylene transfer product and $[Cp_2Ti{=}O]_n$. Alternatively, if the intermediate has a good leaving group in the β-position, products can form by β-elimination of the leaving group from the metallacycle. This type of reactivity is seen in the reaction of **1** with acid chlorides[3] and anhydrides.[4]

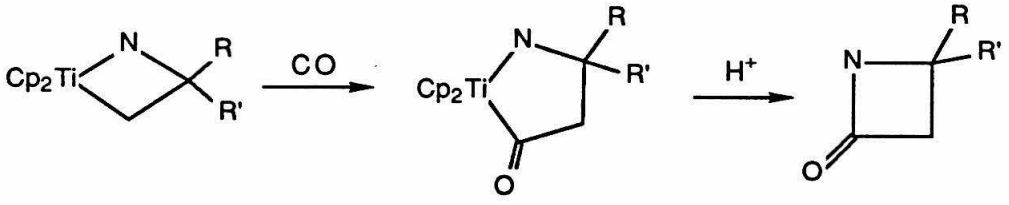
To date, most of the work in this area has concentrated on the olefin metathesis reaction[5] and the reactivity of **1** with carbonyl-containing compounds.[2] In order to more fully understand the mechanisms of these reactions, it is desirable to identify intermediates in the processes. Identification of such species can be attained through isolation or spectroscopic observation. In the case of olefin metathesis, many titanacyclobutanes have been isolated and characterized spectroscopically and crystallographically.[6] Conversely, in the reaction with ketones, for example, there is a much higher driving force for the intermediate to form products, thus precluding the detection of any intermediate. The formation of a Ti=O bond is a very thermodynamically favored process, making this reaction rapid and irreversible. Olefin metathesis is reversible with the position of equilibrium determined by the relative stabilities of the metallacycles and alkenes.[7] It is presumed that the reactions of **1** with acid chlorides and anhydrides also go through this type



Scheme 1. Reactivity of titanocene methylidene with C=X multiple bonds and reaction pathways taken by resulting intermediates.

of cyclic intermediate that subsequently β-eliminates a chloride or a carboxylate, respectively. Although it is surprising that such a β-elimination would be favored kinetically or thermodynamically over cleavage of the oxa-metallacycle to produce the methylene transfer product and $[Cp_2Ti{=}O]_n$, there is no evidence that supports any alternative mechanism.

An aza-metallacycle, on the other hand, might be more stable than an oxa-metallacycle because of a reduced driving force to form a Ti=N bond. Therefore, this intermediate might be detected spectroscopically or possibly isolated. If this type of species could be isolated or generated *in situ*, it could potentially be used for generating nitrogen-containing organic compounds. Carbonylation and protonolysis of an aza-metallacycle would be expected to produce a lactam. (See Equation 1.) This chapter describes the reaction of **1** with some selected compounds containing a C=N bond.

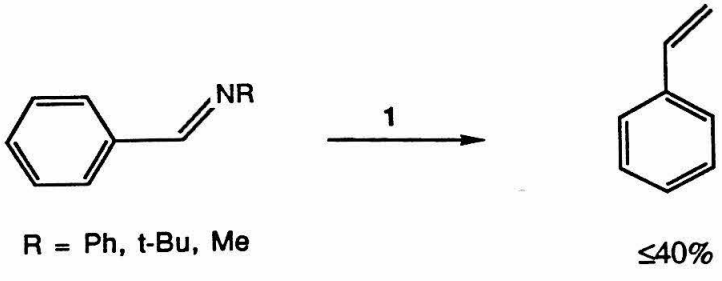


(1)

RESULTS AND DISCUSSION

The Reaction of Titanocene Methylidene with Imines

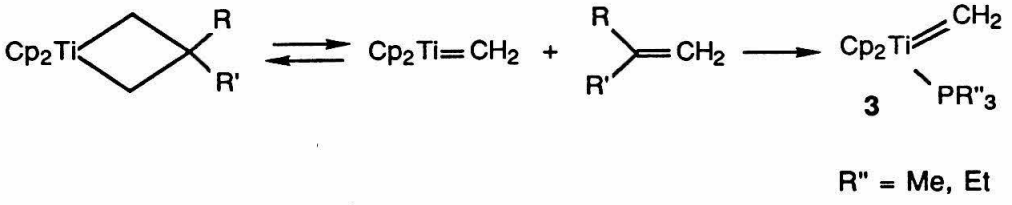
In order to determine the reactivity of titanocene methylidene with compounds containing the C=N moiety, selected imines were examined as substrates. (See Equation 2.) The reduced driving force to form a Ti=N bond should make an aza-metallacycle more stable than the oxa-metallacycle intermediate that is formed in the reaction with ketones. The reaction conditions were similar to those used in the preparation of titanacyclobutanes. A THF or toluene solution of a β,β-disubstitiuted titanacyclobutane[1] at 0 °C was treated with the imine. After a period of stirring at 0 °C, the temperature was reduced to −20 °C, and solvent was removed *in vacuo*. It was found that the reactivity of imines is analogous to that of ketones; the only product isolated was the alkene formed from methylene transfer. The reactions with imines are not as clean as those with ketones, and the yields of alkenes formed are not as high. In most cases, they are on the order of about 40%. The low yields could be due to polymerization of styrene, the alkene produced in the reaction. No aza-metallacycle or any other identifiable organometallic product was isolated under these conditions.



(2)

The reaction was repeated using Tebbe's reagent as the source of **1** with the progression of the reaction monitored by NMR at reduced temperature. It was

believed that the reduced temperature might slow the rate of aza-metallacycle cleavage and allow for observation of, if not isolation of, an intermediate. Both toluene-d_8 and THF-d_8 were used as solvents in repeated attempts. These attempts proved to be unsuccessful. During the course of the reaction, the NMR signals became broadened, so it was difficult to gain any useful information from these experiments. There were no new cyclopentadienyl signals, the appearance of which would indicate the presence of a new organometallic product. The solution eventually turned green and appeared to be paramagnetic.



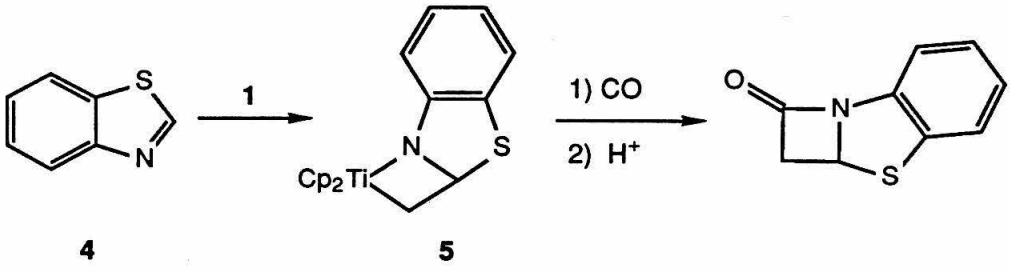
(3)

Finally, it was thought that even if the intermediate could not be observed, perhaps some novel titanocene imido products might be isolated from the methylene transfer reaction. It had been seen earlier that titanocene methylidene could be trapped from the metathesis reaction. This species has been trapped by various phosphine ligands.[8] (See Equation 3.) The first attempt at adding a phosphine to the reaction mixture was unsuccessful. Apparently, titanocene methylidene reacts faster with an incoming phosphine ligand than the imine because the only product isolated was the phosphine adduct of titanocene methylidene **3**. Another approach was to add the phosphine trapping agent later in the course of the reaction, so that titanocene methylidene would not be trapped by phosphine before reacting with the imine. The reaction was also run in THF rather than in an

aromatic solvent. It had been noted that $[Cp_2Ti{=}O]_n$, the final organometallic product formed in reactions with carbonyl-containing compounds, appears to be more soluble and less aggregated in polar solvents. The use of a polar solvent should facilitate trapping of a monomeric titanocene imido complex. However, no tractable organometallic products were isolated. It has not been determined if it is instability, aggregation, or polymerization that prevents isolation or detection and characterization of organometallic products.

Heterocyclic Compounds Containing a C=N Bond

In stability studies on titanacyclobutanes, it has been found that metallacycles formed from cyclic olefins are more stable than those formed from non-cyclic internal ones.[7] In an analogy to this finding, it was thought that a heterocyclic compound containing a C=N bond might have a better chance of forming a stable aza-metallacycle. The first substrate of this type to be examined was benzothiazole **4**. Carbonylation of the aza-metallacycle **5** that would be expected to form from this compound could potentially produce an interesting β-lactam. (See Equation 4.)



4 **5** (4)

Treatment of a red solution of **1** (from β,β-dimethyltitanacyclobutane[1]) with an equivalent of benzothiazole in an NMR tube reaction in benzene-d_6 at room

temperature caused a color change to emerald green. Usually a color change from red to green indicates a reduction of Ti(IV) to Ti(III). Recording the NMR spectrum of this reaction mixture showed a new organometallic product with sharp signals. The pattern of signals did not appear to be consistent with the expected tricyclic product **5**. Nevertheless, it appeared to be a clean reaction with quantitative production of a new organometallic product and isobutylene. From the pattern of NMR signals, which appeared to be those for 10 cyclopentadienyl protons, four aromatic protons and three protons for a vinyl group, the product was postulated to be compound **6**. The 500 MHz ^{1}H NMR spectrum of the compound is shown in Figure 1.

The formation of this unusual looking product seen in this reaction can be rationalized by the formation of an intermediate aza-metallacycle, followed by irreversible β-sulfide elimination. A mechanism for this transformation is outlined in Scheme 2. This mechanism is analogous to that proposed for other apparent β-eliminations from intermediate metallacycles. The reaction is rapid, so no intermediates could be detected spectroscopically at room temperature. Using Tebbe's reagent as the methylidene source and following the reaction at -50 °C, the same rapid quantitative formation of **6** was observed with no discernible accumulation of the proposed intermediates **7** or **8**.

When this reaction is carried out on a preparative scale, removal of the solvent from the green solution *in vacuo* gave a black powder in 92% isolated yield. Recrystallization of the black powder from dichloromethane-hexane at -20 °C afforded air-stable, green-black crystals suitable for x-ray diffraction.

The crystal structure[9] of this product verified the identity of this compound. It is a bicyclic compound with a five-membered ring containing Ti, S, and N fused to a benzene ring. Two views of this compound are shown in ORTEP drawings in

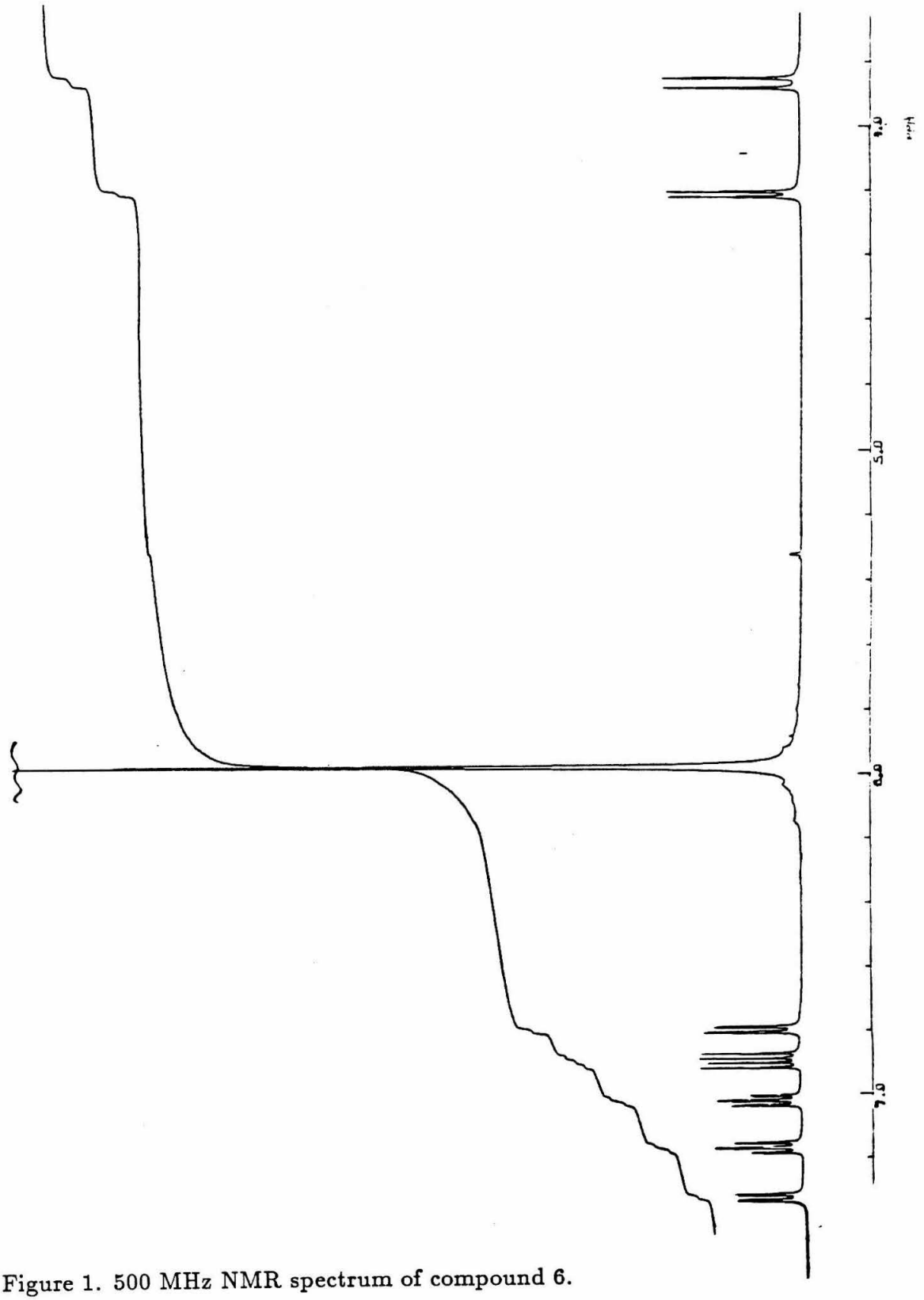
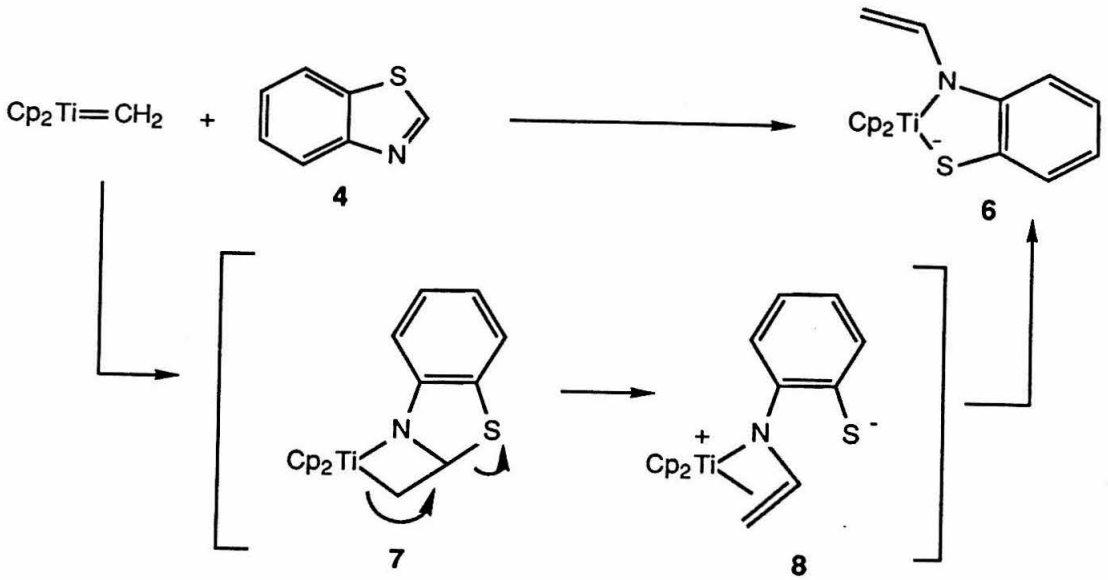


Figure 1. 500 MHz NMR spectrum of compound 6.



Scheme 2. Proposed mechanism for the reaction of titanocene methylidene with benzothiazole.

Figures 2 and 3. Figure 2 shows the bicyclic structure of the compound. The view in Figure 3 shows the metallacycle to be a nonplanar ring in which the $N(C_6H_4)S$ plane of the molecule was folded out of the N-Ti-S plane by 38°. The nonplanar geometry is similar to that seen in other similar d^0 organometallic compounds such as enedithiolates,[10] enediolates,[11] eneamidolates,[12] and s-*cis*-diene complexes.[13] A $\sigma^2\pi$ bonding mode has been suggested to account for the folding of the chelate ring.[14]

The temperature dependence of the NMR spectrum shows **3** to be a fluxional molecule. At room temperature, there was one averaged signal for the cyclopentadienyl rings. When the temperature was lowered to −100 °C, two slightly broadened singlets of equal intensity for nonequivalent cyclopentadienyl rings were observed, indicating the presence of two conformers. These conformers are interconverted presumably by folding along the S···N axis. From the coalescence

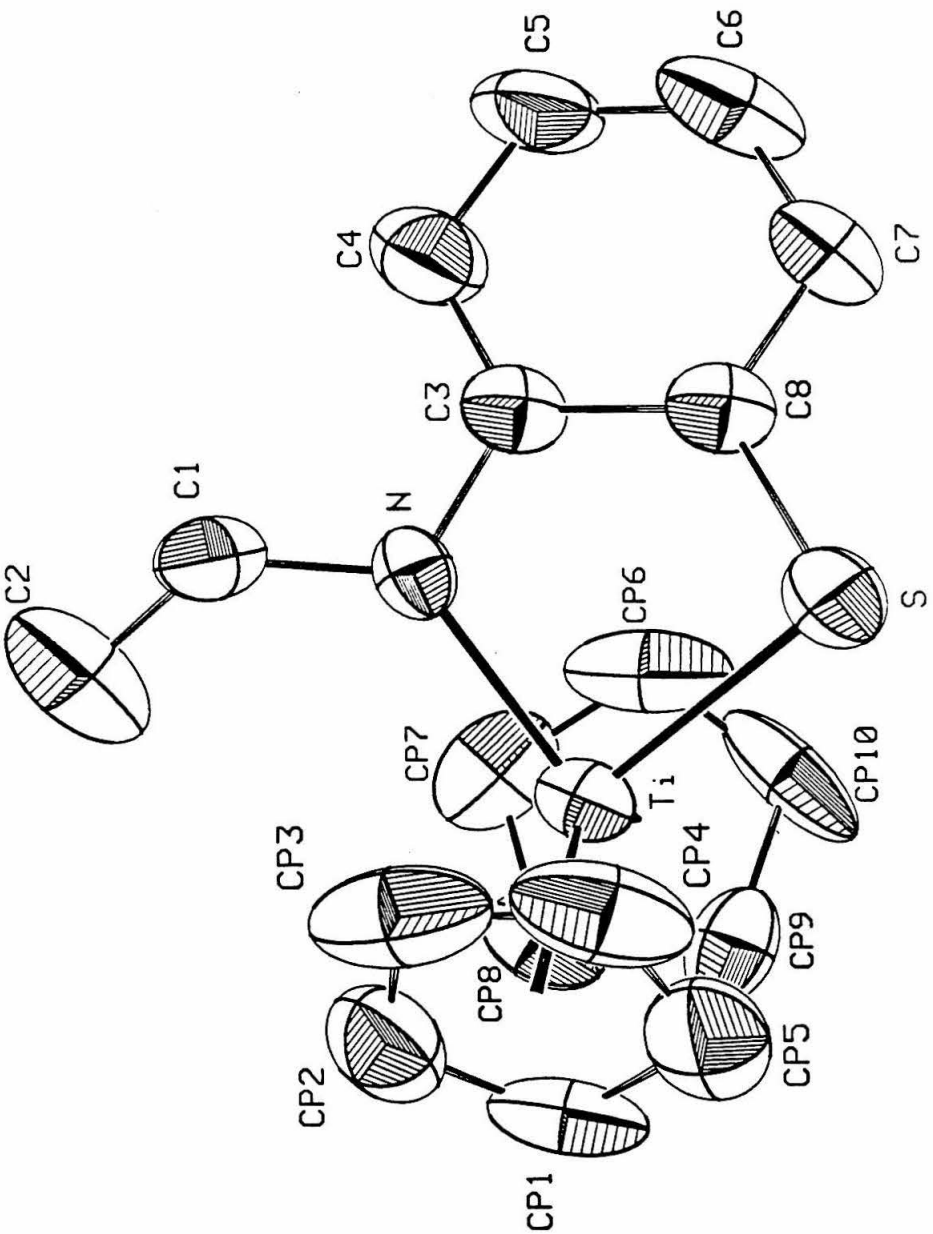


Figure 2. ORTEP Drawing showing bicyclic structure of **6**.

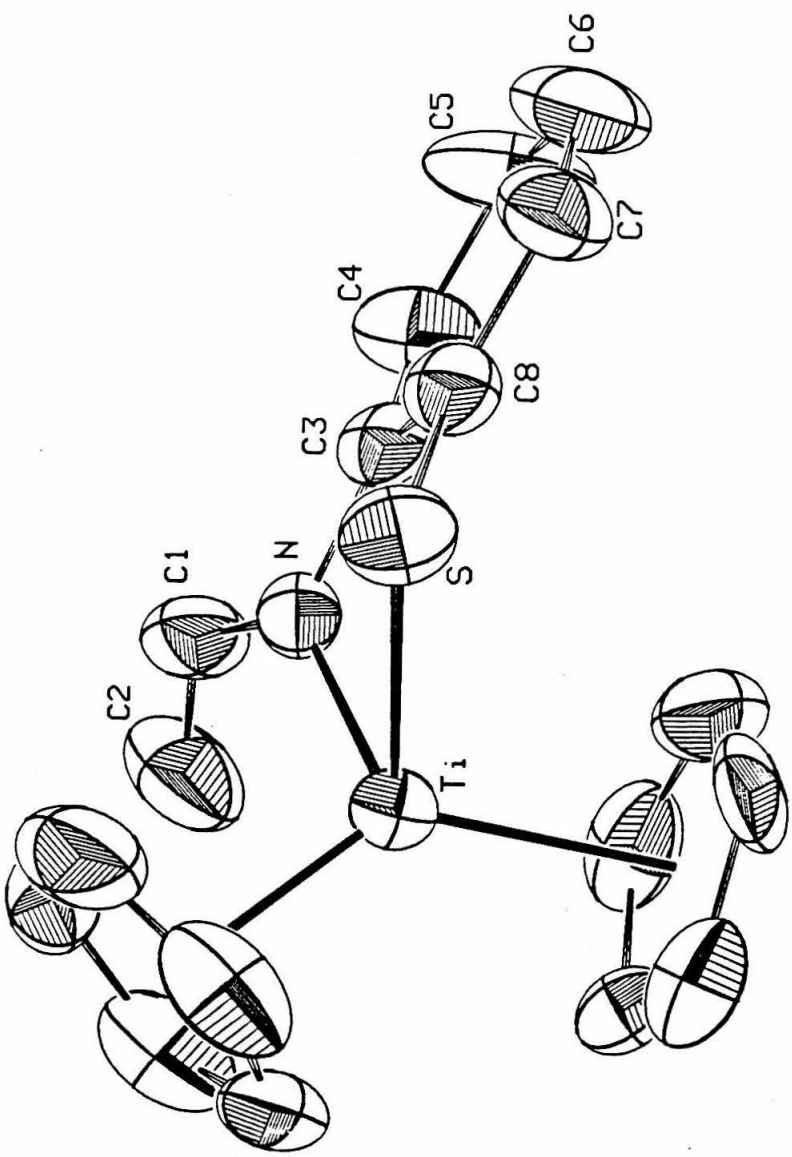


Figure 3. ORTEP drawing showing nonplanar metallacycle in **6**.

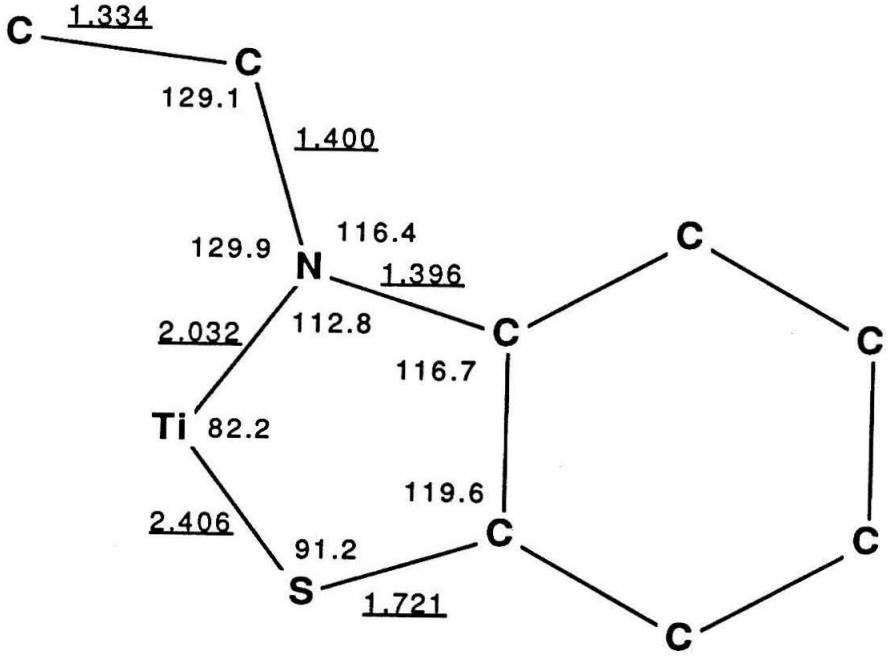
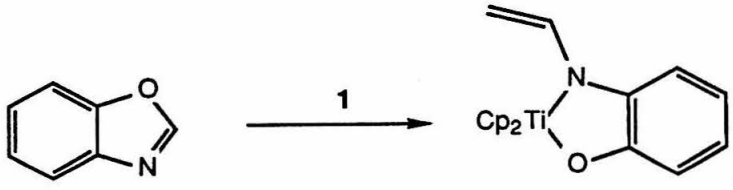


Figure 4. Selected bond lengths (Å, underlined type) and angles (°).[16]

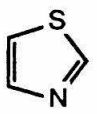
temperature T_c (−68 °C) and the signal splitting $\Delta\nu$ (67 Hz), the approximate value of the free energy of activation $\Delta G^{\ddagger}$ for this process is calculated[15] to be 9.8 (±0.5) kcal mol^{-1}. This inversion barrier is less than 14 kcal mol^{-1}, the value reported for the corresponding dithiolate.[9] In this compound, the planar nitrogen may facilitate lowering the barrier to interconversion. Figure 4 shows a number of selected bond lengths and angles. It can be seen that the angles around nitrogen total 359.1°, making it almost completely planar.

A similar heterocycle, benzoxazole **9**, appears to react in much the same way with a β-phenoxide elimination from the aza-metallacycle. The product of this reaction **10** is characterized by its NMR spectrum, which is nearly identical to that of **6**. (See Equation 5.) It is a quite unstable compound, resistant to isolation in pure form. The instability of **10** contrasts with **6**, which is stable for at least three years in the drybox. Another difference in this compound is that if it exhibits any fluxional behavior, it cannot be detected in its NMR spectrum at temperatures as low as −100 °C.

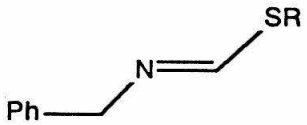


9 **10** (5)

As with the reaction of titanocene methylidene with alkenes, the reaction with C=N containing heterocycles is quite sterically sensitive. There is no reaction when



11



12: R = Ph
13: R = CH_2Ph

1-methylbenzothiazole is treated with **1**. Thus, a single methyl group can stop an otherwise fast, quantitative reaction.

Although the reaction of titanocene methylidene with benzothiazole is quite fast and quantitative, this type of reaction is not general for other similar molecules. For example, treatment of a titanacyclobutane or Tebbe's reagent at low temperature with thiazole **11** results only in the decomposition of the titanocene methylidene source. In an attempt to determine if better leaving groups were necessary for the β-sulfide elimination step, the *S*-arylformimidates **12** and **13** were prepared. These compounds also failed to produce any tractable organometallic product. The problem with these compounds is presumably sterics. The fused phenyl ring on benzothiazole provides a good leaving group for the β-sulfide elimination in contrast to thiazole. On the other hand, the *S*-arylformimidates have good leaving groups, but their phenyl rings are unconstrained and can freely rotate. This probably creates more steric interaction between these groups and the cyclopentadienyl rings. The fact that the *S*-arylformimidates also exist predominantly as the *Z*-isomer[15] probably also inhibits the reaction. This is in analogy to the fact that titanocene methylidene will react faster with cyclic *cis*-alkenes than with noncyclic *trans*-alkenes. It appears that of the substrates examined, benzothiazole has just the right combination of steric and electronic characteristics that allows for the formation of a metallacycle with β-elimination of a good leaving group as seen with other substrates such as acid chlorides and anhydrides.

SUMMARY

The reaction of titanocene methylidene with imines does not form stable aza-metallacycles. They appear to react in the same way as ketones and simply undergo methylenation with no observable intermediates. However, this is a low-yield reaction that does not appear to be synthetically useful. Attempts at isolating any titanocene complexes were unsuccessful.

The heterocyclic compounds, benzothiazole and benzoxazole, react with titanocene methylidene to form what are proposed to be similar aza-metallacycles which then undergo a β-elimination to form novel metallacycles. This reaction is not general for other similar but noncyclic compounds with the N=C–S linkage. However, the reactions with these heterocycles are interesting examples that support the proposed mechanism of β-elimination of good leaving groups from an intermediate metallacycle.

EXPERIMENTAL SECTION

General Considerations. All manipulations of air- and/or water-sensitive compounds were performed using standard high-vacuum or Schlenk techniques. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). Compounds were transferred and stored in a nitrogen-filled Vacuum Atmospheres glovebox, equipped with an MO-40-1 purification train, DK-3E Dri-Kool conditioner, and Dri-Cold freezer. Flash chromatography was performed by the procedure of Still[18] using Woelm 32-63 (32-63 μ m). Thin layer chromatography was performed on EM Reagents 0.25 mm silica gel 60-F plates and visualized with either iodine vapor or phosphomolybdic acid/ethanol spray. All reaction temperatures were measured externally.

Materials. Toluene, diethylether, and tetrahydrofuran were stirred over CaH_2, then transferred to purple sodium-benzophenone ketyl. Pentane and hexane were stirred over concentrated H_2SO_4, washed with H_2O, dried over CaH_2, then transferred to purple sodium-benzophenone ketyl with tetraglyme. Dichloromethane was stirred over P_2O_5 or CaH_2 and degassed by evacuation of freeze-pump-thaw cycles. Dried degassed solvents were vacuum-transferred into dry glass vessels equipped with Teflon valve closures and stored under argon. Benzene-d_6, toluene-d_8, and tetrahydrofuran-d_8 (Cambridge Isotopes) were dried and vacuum-transferred from purple sodium-benzophenone ketyl. Chloroform-d (Aldrich) was dried over 4 Å molecular sieves. Dichloromethane-d_2 (Cambridge Isotopes and Norell, Inc.) was dried over CaH_2 and degassed by several freeze-pump-thaw cycles. All other materials not otherwise specified were obtained from Aldrich and used without further purification.

Instrumentation. NMR spectra were recorded on a Varian EM-390 (90 MHz, ^{1}H), JEOL FX-90Q (89.60 MHz, ^{1}H; 22.53 MHz, ^{13}C), JEOL GX-400

(399.65 MHz, ^{1}H; 100.4 MHz, ^{13}C) or Brüker WM-500 (500.13 MHz,^{1}H). Chemical shifts are reported in δ, referenced to residual solvent signals (^{1}H: C_6D_6, δ 7.15; C_7D_8, δ 2.09; THF-d_8, δ 3.58 or 1.73; CD_2Cl_2, δ 5.32; $CDCl_3$, δ 7.24; ^{13}C: C_6D_6, δ 128.0; C_7D_8, δ 20.9; THF-d_8, δ 67.4; $CDCl_3$, δ 77.0).Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), coupling constant (Hz), integration and assignment. Gas chromatography analyses were performed on a Shimadzu GC-Mini-2 equipped with an SE-30 capillary column, flame-ionization detector, and a Hewlett-Packard 3390A integrator.

General procedure for NMR tube reactions

The titanacyclobutane or Tebbe's reagent was loaded into a tared NMR tube. Benzene-d_6, toluene-d_8, or THF-d_8 (350-400 μl) was added to the tube; the latter two solvents were used for variable temperature NMR spectroscopy experiments. A latex septum was fitted onto the tube, and it was sealed with Parafilm. Liquid substrates and internal standards were added *via* syringe.

Attempted preparation of aza-metallacycles with titanocene methylidene and imines

Using titanacyclobutanes. To a solution of 1.1 equiv of a titanacyclobutane in THF or toluene was added 1.0 equiv of imine. After about 10 min, the color of the solution had changed from red to brown. At this time, the solution was cooled to -20 °C, and the solution was concentrated *in vacuo*. Analysis of the crude product showed only alkene produced from methylene transfer and intractable organometallics.

Using Tebbe's reagent. To a -40 °C solution of 1.1 equiv of Tebbe's reagent in THF was added 1.0 equiv of the imine. Over 10-20 min the solution went

from red to brown. Concentration of this solution at −40 °C failed to produce an aza-metallacycle.

Preparation of metallacycles 6 and 10

To a solution of 1.1 equiv of a titanacyclobutane at 0 °C was added 1.0 equiv of the appropriate heterocycle. This solution was then allowed to warm to room temperature. The reaction was complete after 5-10 min, at which time the solution was concentrated. The reaction with benzothiazole produced a black powder in 92% yield. The black powder was dissolved in a minimum amount of dichloromethane and layered with hexane. This solution was transferred to the −20 °C freezer. This recrystallization produced sparkly, green-black crystals suitable for x-ray diffraction.[9,15] mp 177-180 °C; ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.32 (dd, J=1.52 Hz, J=7.5 Hz, 1H), 7.17 (ddd, J=1.2 Hz, J=7.5 Hz, J=6.2 Hz, 1H), 7.02 (ddd, J=8.2 Hz, J=1.5 Hz, J=6.2 Hz, 1H), 6.89 (dd, J=8.0 Hz, J=15.1 Hz, 1H), 6.79 (dd, J=1.2 Hz, J=8.2 Hz, 1H), 6.03 (s, 10H), 4.21 (dd, J=8.0 Hz, J=0.5 Hz, 1H), 3.87 (dd, J=15.1 Hz, J=0.5 Hz, 1H); ^{13}C NMR (90 MHz, CD_2Cl_2): δ 147.1, 129.6, 125.6, 122.2, 116.3, 111.6, 99.3.

The reaction with benzoxazole produced a brown-black, waxy material. This material was also very unstable. Attempts at recrystallization were fruitless, resulting in decomposition of the compound. ^{1}H NMR (90 MHz, CD_2Cl_2): δ 6.84-7.52 (m, 5H), 6.13 (s, 10H), 4.06 (d, J=7.2 Hz, 1H), 3.76 (d, J=14.4 Hz, 1H); ^{13}C NMR (90 MHz, CD_2Cl_2): δ 144.3, 129.5, 126.3, 124.6, 123.1, 115.9, 111.8, 100.0.

Preparation of thioformanilide[19]

A solution of 3.59 g (29 mmol) N-phenylformamide in 80 ml of acetonitrile was prepared at room temperature. To this was slowly added 10 g (45 mmol) of P_2S_5 and then 3.8 g (45 mmol) of $NaHCO_3$. The opaque yellow solution changed to clear yellow as the reaction mixture was allowed to stir at room temperature

overnight. After removal of the solvent *in vacuo*, the residue was dissolved in Et_2O. This solution was washed with H_2O (4 × 25ml), dried ($MgSO_4$), and concentrated to yield a yellow solid. The crude product was recrystallized from dichloromethane to give 3.4 g of white needles. (85% yield) ^1H NMR (90 MHz, C_6D_6): δ 9.47 (br s, 1H), 6.70-7.01 (m, 3H), 6.10-6.42 (m, 2H).

Preparation of *S*-alkylthioformimidates 12 and 13[15]

A suspension of 1.5 equiv of NaH was prepared in THF at room temperature. To this was slowly added 1.0 equiv of the appropriate alkyl halide, and the reaction was stirred at room temperature for 1 h. The white precipitate was filtered off, and the solution was concentrated. When bromobenzene was added as the alkyl halide, concentration yielded a yellow oil that was crystallized from dichloromethane-hexane. ^1H NMR (90 MHz, C_6D_6): δ 8.52 (s, 1H), 6.48-7.20 (m, overlapping with solvent).

When benzyl bromide was used as the alkylating agent, concentration gave a thermally labile yellow oil that was pure enough by NMR analysis to be used without further purification. ^1H NMR (400 MHz, C_6D_6): δ 8.52 (s, 1H), 6.91-7.57(m, overlapping with solvent), 4.39 (s, 2H).

Treatment of titanocene methylidene with *S*-arylformimidates and thiazole

The reactions with these substrates were conducted in the same manner as those with imines, with the same poor results. There was never any evidence of any aza-metallcycle formation, with or without β-sulfide elimination.

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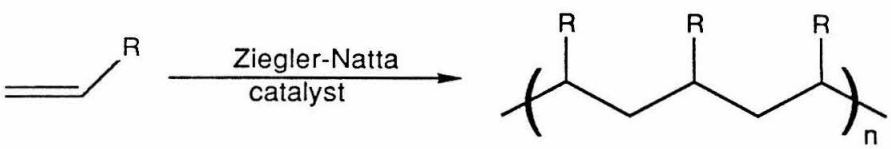
Chapter 4

Elementary Steps in a Soluble Model Ziegler–Natta Polymerization System

INTRODUCTION

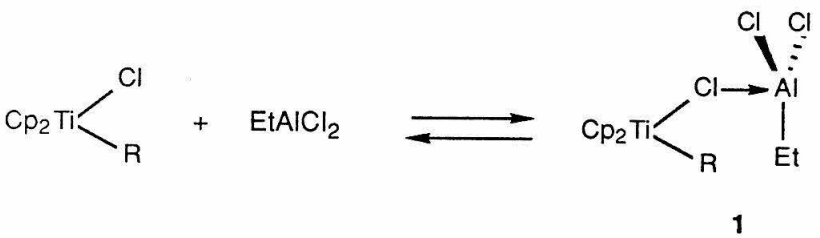
Ziegler–Natta polymerization[1] of ethylene and α-olefins (see Equation 1) with catalysts formed from the combination of a transition metal compound and a main group alkyl halide is an important commercial process, producing many millions of tons of polyolefins annually. For large scale industrial processes, heterogeneous systems are used because of their high efficiency and low cost. However, homogeneous systems such as titanocene derivatives with alkyl aluminum chlorides have received a great deal of attention in the academic literature because they are more amenable for the study of mechanistic details. The homogeneous systems are easier to study because the nature of the catalyst precursor can be more clearly elucidated through spectroscopy and other classical analytical techniques. Much work has been done in an attempt to establish the mechanism of the elementary steps in Ziegler–Natta polymerization. The study of these steps—initiation, propagation, and termination—are of interest because the properties of the resulting polymers are determined by these processes. In this section, we will briefly outline some of the individual steps in the process and some of the work done in studying them in homogeneous systems. We have designed a uniquely modified version of the well studied homogeneous titanocene catalysts to further explore some of these fundamental steps.



(1)

In all the known Ti/Al systems containing at least one chlorine ligand per titanium, there is a very rapid complex formation **1** evidenced by color intensification.[2]

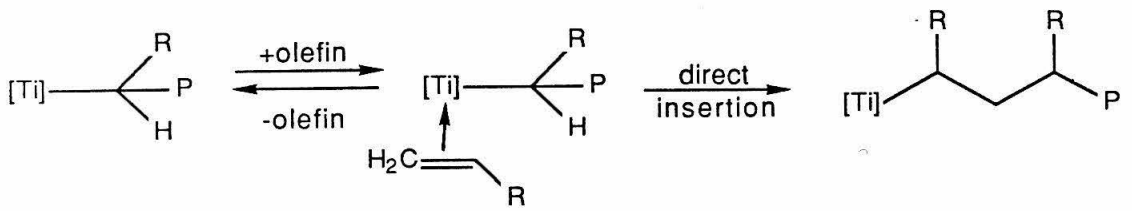
(See Equation 2.) These complexes have not been isolated and have been identified only spectroscopically. A complex having electron-deficient bonding at the titanium center is postulated as the transition state. The actual character of both this active site and also the transition state in the olefin insertion reaction remains a topic of debate.[3]



(2)

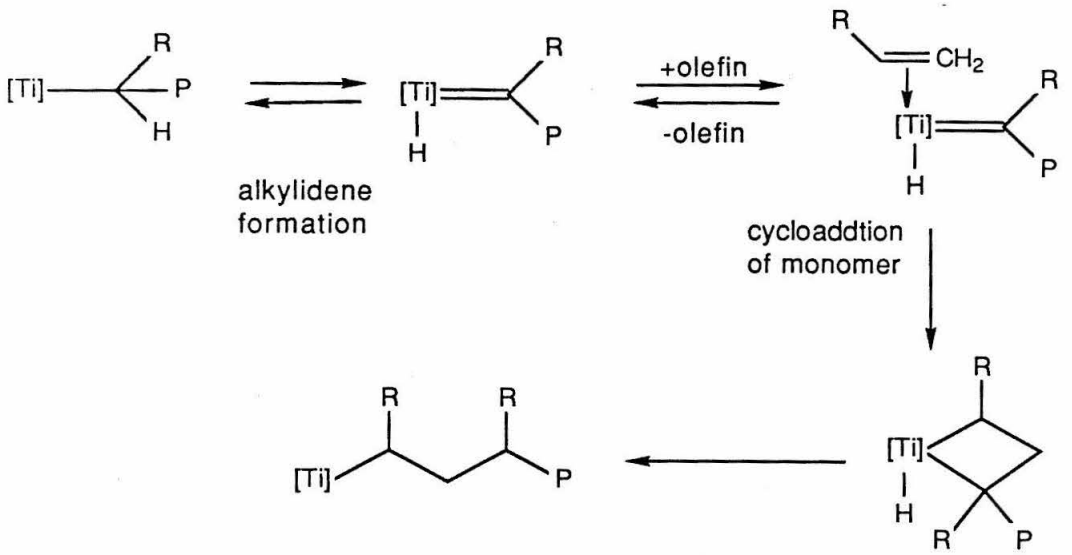
1

Central to the topic of Ziegler–Natta polymerization is the addition of a monomer unit to the growing polymer, the propagation step. The direct insertion of an olefin into a metal–carbon bond has been postulated to be the major pathway in this process as well as other transition-metal-catalyzed reactions forming C–C bonds. The direct insertion of the olefin is referred to as the Cossee–Arlman mechanism.[4] (See Scheme 1.) This mechanism has drawn some criticism because of the rare number of cases where this key step has been directly observed in structurally well-defined systems. The existence of this type of insertion has been inferred from the isolation of secondary products arising from further insertion, as in the case of olefin polymerization, or decomposition *via* β-hydrogen or β-alkyl elimination. Even though there have been quite a few *cis*-alkyl ethylene compounds isolated, none have been shown to undergo olefin insertion into the metal–alkyl bond.[5] One well-defined system in which olefin insertion can be directly detected has been reported by Watson,[6] who observed the direct insertion of propene into a Lu–CH_3 bond.

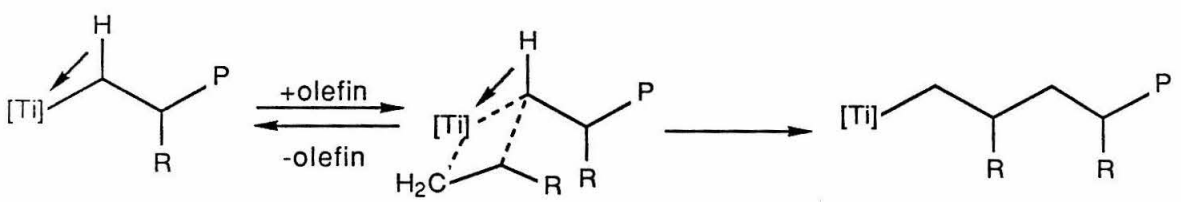


Scheme 1. Cossee-Arlman mechanism of direct insertion.

An alternative mechanism for monomer addition has been advanced by Green and co-workers.[7] Both the original and modified versions of this mechanism are outlined in Scheme 1. The original proposal is based in part on the observation that catalyst precursor components are similar for many Ziegler–Natta and olefin metathesis systems. This mechanism is very similar to the well-known metathesis mechanism. The first step in this mechanism is an α-hydrogen abstraction to form an alkylidene which then undergoes a [2+2] cycloaddition to form a metallacycle as in the olefin metathesis reaction.[8] This intermediate undergoes reductive elimination. Propagation follows from the formation of another alkylidene, cycloaddition, reductive elimination and so on. The proposal was revised,[9] so that instead of a hydride shift, there is a 3-center, 2-electron bond in which the electron density in one of the α-carbon–hydrogen bonds is donated to the metal center. This type of complex is proposed to be an analogue to the transition state of α-hydrogen abstraction. Schrock[10] has reported a tantalum-based polymerization system that supports this theory. In addition to providing an alternative mechanism for olefin insertion, they propose that this scheme also could account for any stereospecificity seen in α-olefin polymerization in soluble catalyst systems.

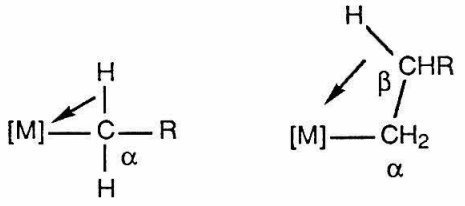


original Green-Rooney Mechanism



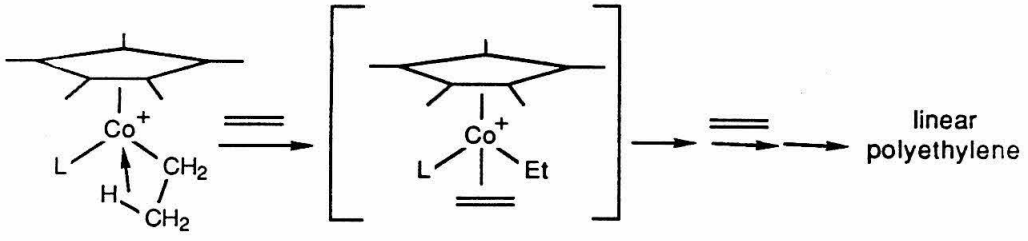
modified Green-Rooney Mechanism

Scheme 2. Two versions of the Green-Rooney mechanism of olefin addition.



3-center, 2-electron bonds

Another proposal involving the interaction of the metal center with a carbon-bonded hydrogen is one put forth by Brookhart[11] and Orpen[12] from their independent work on similar cobalt complexes. Each of these complexes contains an ethyl group with a bridging β-hydrogen. This bridging hydrogen distorts the ethyl group so that it is intermediate in structure between that of a normal ethyl group and an ethylene hydride. Their hypothesis states that factors which favor a bridging hydride over a terminal one will facilitate olefin insertion and that the ethylene alkyl analogues of these compounds should undergo facile migratory insertion. They find that when these compounds are treated with ethylene, insertion occurs rapidly, so that detection of an ethylene alkyl complex **2** is precluded. (See Equation 3.)

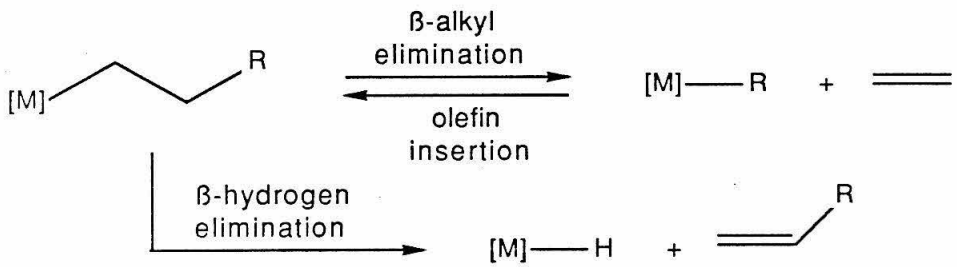


(3)

2

L = $P(OMe)_3$, $P(p\text{-tolyl})_3$

Information about olefin insertion, the key reaction in Ziegler–Natta polymerization, can also be gained from the study of its microscopic reverse, β-alkyl elimination. (See Equation 4.) In sharp contrast to the widespread occurrence of β-hydrogen elimination, there have been only a few reports of β-alkyl elimination. The scarcity of examples is most likely due to the propensity with which metal alkyls undergo β-hydrogen elimination, often irreversibly. Therefore, in order for β-alkyl elimination to occur, there must be an increased driving force such as the release of strain energy or removal of steric congestion around the metal center, and an inhibition of β-hydrogen elimination.

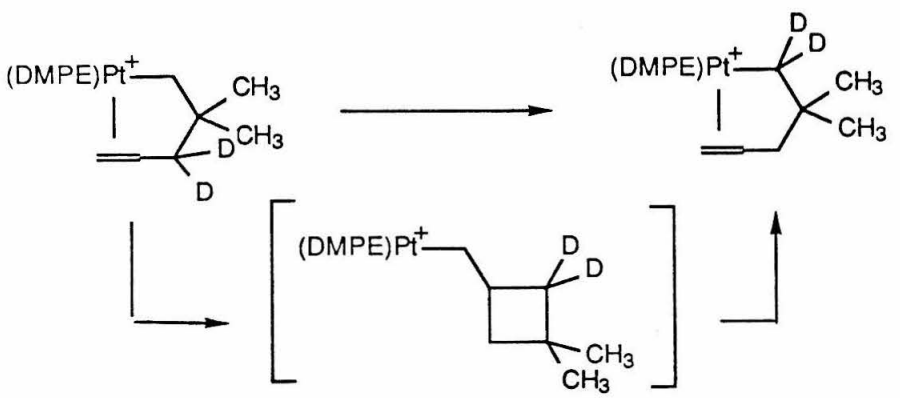


(4)

Watson[13] has reported β-alkyl elimination from $(C_5Me_5)_2LuCH_2CH(CH_3)_2$, the product of propene insertion into a Lu–CH_3 bond. In this system, β-hydrogen elimination is competitive with this process but appears to be less favorable, presumably because of steric congestion that develops in the transition state (vide infra).

Other examples of β-alkyl elimination have been observed in platinum and scandium complexes. Flood[14] has reported the isomerization of a deuterium-labelled platinum compound that isomerizes through an apparent reversible olefin

insertion/β-alkyl elimination process. (See Equation 5.) The intermediate insertion product **3** was not observed. In a similar compound,[15] a platinum cyclobutyl methyl compound undergoes β-alkyl elimination to form the pentenyl complex. Bercaw and co-workers[16] have reported a series of permethylscandocene derivatives that undergo β-alkyl elimination, reversibly in some cases. All these scandium compounds have β-hydrogens, but β-hydrogen elimination is also thought to be less favorable because of unfavorable steric interactions in the transition state.

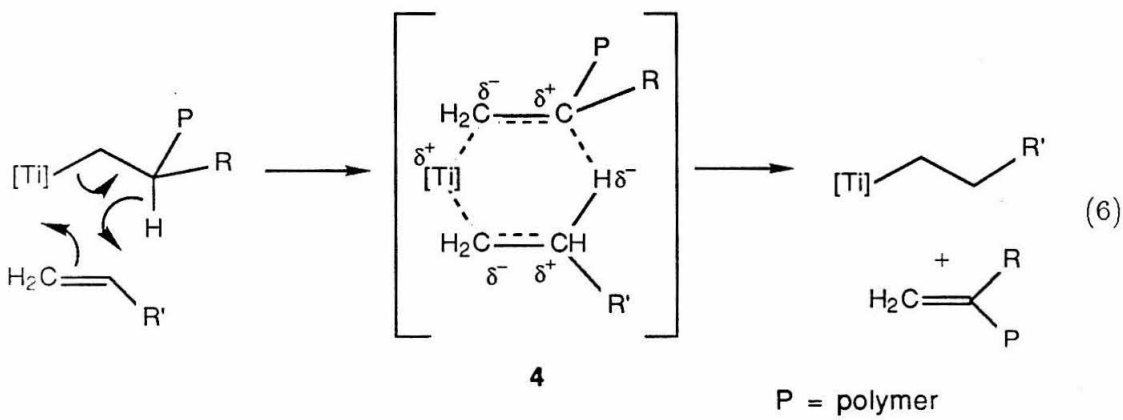


(5)

3

The polymerization of α-olefins, promoted by homogeneous Ziegler–Natta catalysts based on Ti(IV) compounds and aluminum alkyls, occurs simultaneously with other reactions that complicate the study of this process.[1] The understanding of these side reactions is important because they can affect the length and structure of the resulting polymer chain. Also, some of the aging processes that occurs with homogeneous and heterogeneous Ziegler–Natta catalyst systems can be explained with the aid of these side reactions.[1b]

An important step that has received little attention in soluble Ziegler–Natta polymerization is chain transfer. In this process, the particular growing polymer chain is terminated, but the site of polymerization is left ready for monomer addition and the start of a new chain. Industrially, molecular hydrogen is the most widely used transfer agent employed in dictating polymer molecular weight, but nonpolymerizable olefins have been shown to be the most efficient transfer agents.[1] A six-center, transition state as in **4**, involving the α-olefin, was suggested for this process.[17] (See Equation 6.)



4

P = polymer

(6)

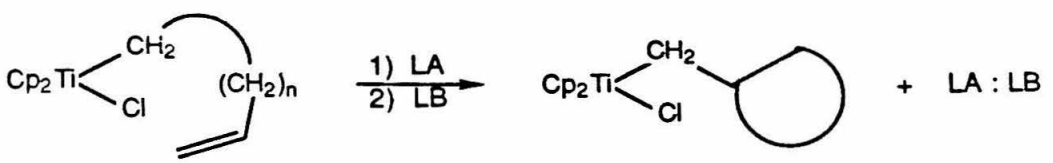
In the following section, we describe the synthesis and study of a series of titanocene alkyl chlorides as a homogeneous model system for Ziegler–Natta polymerization. We have employed titanocene alkenyl chlorides containing a pendant olefin, appropriately situated for intramolecular Lewis acid induced insertion. The intramolecular olefin provides a high local concentration of olefin while maintaining a 1:1 stoichiometry of olefin to metal center. Herein, we discuss the study

of some elementary steps in Ziegler–Natta polymerization, using these and some related compounds. Some aspects of this work have been previously reported.[18]

RESULTS AND DISCUSSION

Olefin Insertion

A series of titanocene alkenyl chlorides were prepared from Cp_2TiCl_2 and the appropriate Grignard reagent. Compounds having alkenyl chains ranging in length from five to eight carbons were used to study the direct insertion of an olefin into a titanium–carbon bond. In this reaction, the pendant olefin undergoes Lewis acid catalyzed intramolecular insertion. (See Equation 7.) In most of the olefin insertion experiments, **6a** was used and treated with a Lewis acid cocatalyst, either $EtAlCl_2$ or Me_2AlCl. Olefin insertion is effected with these aluminum alkyls in toluene at temperatures ranging from −80 °C to −100 °C with $EtAlCl_2$ and in the range of ca. −50 °C to −30 °C with Me_2AlCl.[19] It is important to note that these conditions also effect ethylene polymerization. For example, treatment of **6a** with $EtAlCl_2$ in the presence of ethylene, followed by rapid quenching with HCl/MeOH, resulted in cyclopentyl-capped ethylene oligomers. Capillary GC analysis of the oligomers shows them to be identical to those produced when **6b** is used as the organometallic catalyst. The fact that ethylene is polymerized is significant in that it supports the assertion that the insertion studied is the same type as that observed in Ziegler–Natta polymerization, and that this is a good model for a single monomer insertion.



(7)

n = 2	5a	LA = $EtAlCl_2$	n = 2 5b
3	6a	Me_2AlCl	3 6b
4	7a		4 7b
5	8a	LB = pyridine	5 8b

For comparison, studies were also conducted on a related compound, zirconocene hexenyl chloride **9a**. This compound was prepared by treatment of Cp_2ZrHCl with 1,5-hexadiene. However, the solubility of this compound and its decompostion *via* β-hydrogen elimination prevented its isolation and full characterization. *In situ* preparation of **9a** in an NMR tube reaction with subsequent addition of Me_2AlCl at ambient temperature allows for direct spectroscopic observation of olefin insertion, producing zirconocene cyclopentylmethyl chloride **9b**. Because the zirconocene compounds are not as readily reduced to lower valent species as titanocene derivatives, the reaction can be performed at higher temperatures.

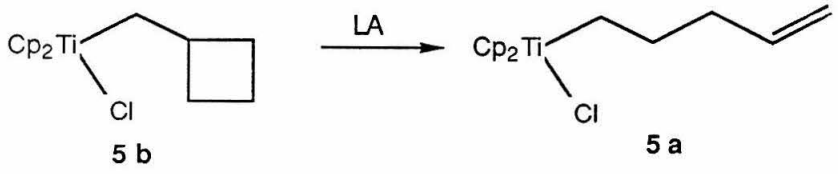
At higher temperatures than those stated earlier, there is a significant amount of reduction in the titanocene compounds, which precludes characterization of the primary transition-metal products. In previous work, this insertion was inferred from analysis of the hydrocarbon products obtained upon hydrolysis of the reaction mixture with HCl/MeOH.[18b,20] However, if the reaction mixture is kept at the prescribed temperature, the primary organometallic insertion product can be isolated. Addition of a Lewis base such as pyridine sequesters the Lewis acid cocatalyst from the titanium product. The solution can then be warmed to room temperature, and the resulting titanocene cycloalkylmethyl chloride can be isolated in high yield. The isolation of the primary insertion product is an important advance in the study of Ziegler–Natta polymerization. It establishes that olefin insertion into the metal–carbon bond is the predominant mechanism. It is one of the few structurally well-defined examples of single monomer addition in an actual Ziegler–Natta polymerization system.

The net result of this reaction is a cyclization of the alkenyl ligand to form a titanocene cycloalkylmethyl chloride, so the rate at which compound undergoes insertion depends on the ease with which the respective cycloalkane is formed. Not

surprisingly, titanocene hexenyl chloride **6a**, which cyclizes to produce the five-membered ring in **6b**, is the most reactive. Titanocene heptenyl chloride **7a** is significantly slower, and cyclization in the pentenyl **5a** and octenyl **8a** compounds is not observed.

β-Alkyl Elimination

To further understand the important olefin insertion step in polymerization, it is useful to study the reverse reaction, β-alkyl elimination. The two titanocene alkenyl chlorides **6a** and **7a** that are observed to undergo olefin insertion apparently do so irreversibly so that β-alkyl elimination cannot be observed.



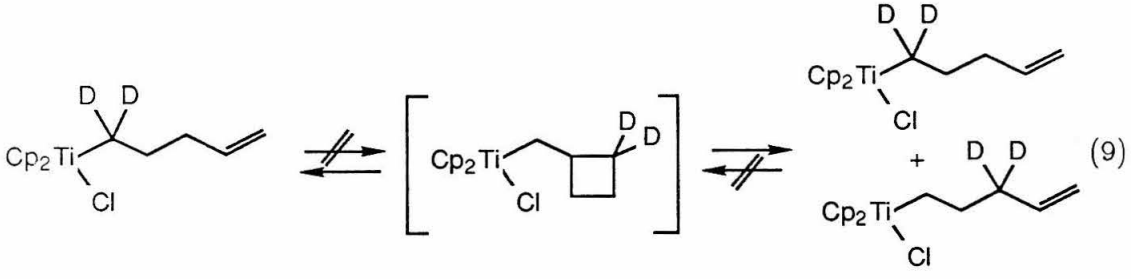
5 b **5 a** (8)

In an attempt to observe β-alkyl elimination, titanocene cyclobutylmethyl chloride **5b** was prepared. This is a system specifically designed to incorporate a high degree of ring strain,[22] which would drive the reaction. Under the identical conditions that effect cyclization in **6a** and **7a**, **5b** undergoes quantitative ring opening *via* β-alkyl elimination. The effects of variables such as Lewis acidity and concentration of the cocatalyst on this process are identical to those observed with olefin insertion.[23]

As in most other examples of β-alkyl elimination, the assumed driving force for the reaction with **5b** is ring strain. An important difference is that the actual species undergoing β-alkyl elimination **5b**, and the primary elimination product **5a** can be both observed and isolated. In this system, the entire process can be followed by NMR spectroscopy. This is an important result because it demonstrates

that this process is an energetically accessible one in homogeneous Ziegler–Natta polymerization.

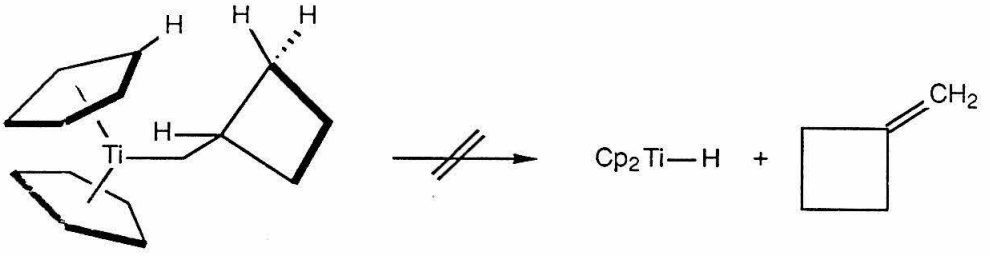
As noted above, the olefin insertion product is not observed with titanocene pentenyl chloride under conditions studied. However, it is possible that the reaction is reversible, but the equilibrium of the reaction lies far enough to the side of the alkenyl compound that the insertion product is not detected. To examine further the possibility of reversibility, the deuterated complex **5a**-α-d_2 was prepared. If cyclization were to take place reversibly, this could be detected by the appearance of deuterium in the γ-position of the pentenyl ligand. (See Equation 9.) However, none of the γ-deuterated pentenyl complex was observed upon treatment of **5a**-α-d_2 with $EtAlCl_2$ for 1-12 h. This result indicates that under these reaction conditions, no cyclization of **5a** occurs. This is in contrast to the Pt system mentioned previously.[14] (See Equation 5.)



(9)

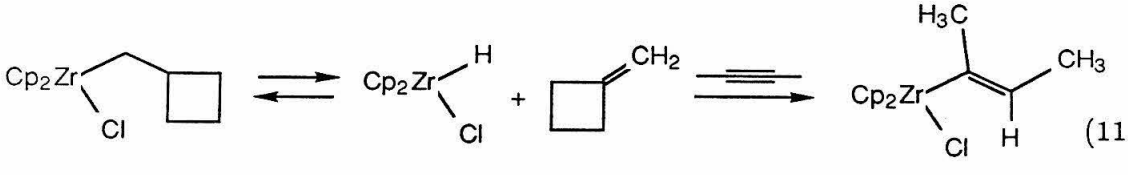
Another difference between this and other systems with β-hydrogens is that β-hydrogen elimination does not compete with β-alkyl elimination. After the completion of the β-alkyl elimination reaction, no free methylenecyclobutane or 1,4-pentadiene is observed. Furthermore, when the reaction is conducted in the presence of excess 2-butyne, there is no trapping of a titanium hydride with release of free alkene, either methylenecyclobutane or 1,4-pentadiene, as would be expected if there was any reversible β-hydrogen elimination occurring. The lack

of β-hydrogen elimination can be rationalized by unfavorable steric interactions in the transition state. In order to achieve the necessary Ti–C–C–H dihedral angle of 0°, the two α-methylene groups would be directed toward the cyclopentadienyl rings. Presumably, this unfavorable transition state precludes β-hydrogen elimination. (See Equation 10.)



(10)

In contrast, the zirconocene cyclobutyl complex **10** prepared by treating methylenecyclobutane with zirconocene hydridochloride does not afford the β-alkyl elimination product upon treatment with a Lewis acid under standard conditions. Not surprisingly, the original olefin insertion reaction is reversible as evidenced by trapping of the hydride in the presence of 2-butyne.[24] (See Equation 11.)



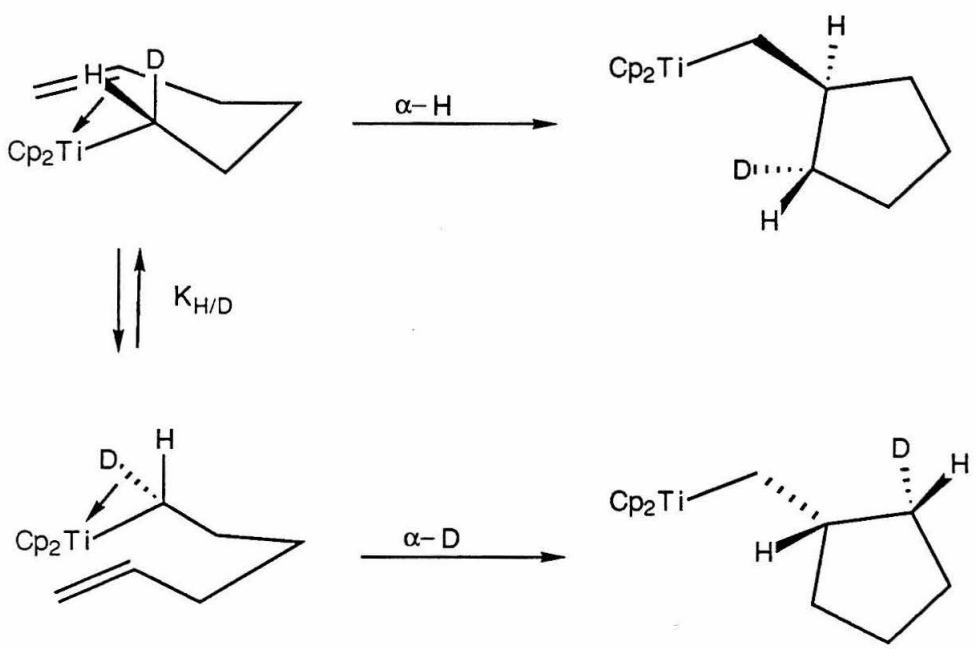
(11)

α-Hydrogen Interaction

The titanocene alkenyl chlorides that were shown to undergo intramolecular olefin insertion were deuterium-labelled with a single deuterium on the α-methylene group. These labelled compounds were used to probe the extent of α-hydrogen interaction with the metal center in olefin insertion in this system as suggested by both versions of the Green–Rooney mechanism. This labelled system has been developed to show an isotope effect on the stereochemistry of olefin insertion if the α-hydrogens are involved in this key reaction, because the stereochemistry is set in the carbon–carbon bond forming step. This insertion of an α-olefin into a Ti–C bond occurs under polymerization conditions, so the measurement of an isotope effect on the stereochemistry of polymerization may be accomplished. This is a direct method to probe for such a C–H interaction.

Insertion of an α-olefin into a metal–alkyl bond that is monodeuterated at the α-postion generates diastereomers as shown in Scheme 3 for one enantiomer of **6a**-α-d_1. Although there may be a *kinetic* isotope effect in direct insertion as proposed by the Cossee–Arlman mechanism,[25] the *stereochemically* determined isotope effect in this situation should be 1.0 in the absence of α-hydrogen interaction. If the α-hydrogens are involved in activation prior to insertion, the symmetry of the CHD is broken, and one coordination site is filled directing the olefin to insert on the side away from this interaction. Donation of electron density to the metal center would be more likely to come from a C–H bond than from a C–D bond.[26] Consequently, if this process is important, the ratio of the resulting diastereomers should not equal 1.0, so that the extent of α-H interaction would be reflected in the diastereomeric ratio. The measurement of the this ratio is a direct method to probe for potential α-interaction.

This isotope effect on the stereochemistry was measured using **6a**-α-d_1 and **7a**-α-d_1. Olefin insertion proceeds under the standard conditions to give a mixture of *cis* and *trans* diastereomers. The ^{2}H NMR spectrum of the isomeric



Scheme 3. Diastereomers resulting from alpha-hydrogen and -deuterium interaction. Chlorine ligand and aluminum cocatalyst omitted for clarity.

organometallic products, as well as the *cis* and *trans* methylcycloalkanes that result from protonolysis of the organometallic products, are readily distinguishable at 76 MHz. In all cases, the ratio of *cis* and *trans* isomers was equal to 1.0 ± 0.07. These results demonstrate that α-hydrogen activation is not a significant factor in the stereochemistry of this olefin insertion reaction in a polymerization system.

This result supports the direct insertion mechanism of polymerization. It also implies that Ziegler–Natta polymerization and olefin metathesis are far more different processes than they might appear. Here it is important to distinguish between the catalyst precursor system and the actual catalyst. Although the components of the catalyst systems for the two processes do appear similar, the interaction of the components to form the respective *catalyst* are different. It has been determined that α-hydrogen abstraction is the first step leading to the active species in olefin metathesis. However, this is a higher energy process that directs olefin insertion.[8] Depending on the reaction conditions, similar systems can react *via* different pathways.

β-Hydrogen Interaction

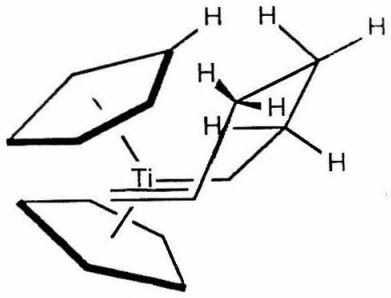
α-Hydrogen interaction was proposed as an explanation for stereoselectivity in homogeneous systems as well as a rationalization for similarities in metathesis and polymerization systems. β-Hydrogen interaction was proposed as being a landmark in transition-metal complexes, indicating a lowered barrier to olefin insertion. If this β-hydrogen interaction is a general phenomenon that can predict the propensity for olefin insertion as predicted by Brookhart,[11] it should certainly be observed in our catalyst system. The method for investigating this is analogous to that used in examining the possibility of α-hydrogen interaction. Compound **6a**-β-d_1 was prepared for such an experiment. As in the previous discussion on α-hydrogen interaction, any β-hydrogen interaction should be reflected in the ratio of diastereomers produced upon olefin insertion.

When **6a**-β-d_1 is treated with a Lewis acid under standard reaction conditions, olefin insertion proceeds as usual. However, the deuterium signals for the diastereomers are not resolved enough to allow for accurate integration in the ^{2}H NMR analysis. It was necessary to separate the signals in order to determine an accurate ratio of the diastereomers. This reaction mixture was treated with *tert*-butyl-hydroperoxide to prepare diasteromeric alcohols. The addition of a shift reagent to the mixture of alcohols shifts the position of the signals, so that they are resolved well enough for the ratio of products to be determined by integration. The 1:1 ratio of observed products indicates that β-hydrogen interaction does not play a role in the olefin insertion in this system.

There is a difference between this system and others in which this β-hydrogen interaction has been observed or proposed. In other systems, the organometallic compound that exhibits a bridging β-hydrogen is quite electrophilic and polymerizes ethylene without the aid of a cocatalyst. In these compounds, the electron density from the bridging hydrogen stabilizes an electron-deficient metal center. This interaction "stores" the unsaturation until contact with ethylene. Titanocene alkenyl (or alkyl) chlorides are stable 16e compounds; the electrophilicity that allows olefin insertion is *induced* by the interaction with a Lewis acid. In these compounds, there is no need for the stabilization that is afforded by the β-hydrogen interaction.

In the presence of an alkyl aluminum cocatalyst, this electrophilic species (perhaps a 14e complex) should be more of a direct analogy to the other electron deficient compounds. However, this compound also has a pendant α-olefin that rapidly inserts, a pathway likely to be preferable to a 3-center, 2-electron C–H interaction. Furthermore, alkyl groups other than ethyl are likely to encounter steric difficulties with a β-hydrogen interaction similar to those shown for β-alkyl elimination in Figure 1. Donation of electron density from one of the β-C–H bonds

into an empty orbital onto titanium requires that the bond be held in the equatorial plane defined by Ti and the ligands in the wedge. As such, the alkyl group on the β-carbon would be directed toward one of the cyclopentadienyl rings. These unfavorable steric interactions could destabilize the metal–hydrogen interaction. It should be noted that this bridging behavior has not been observed or postulated in groups other than ethyl.

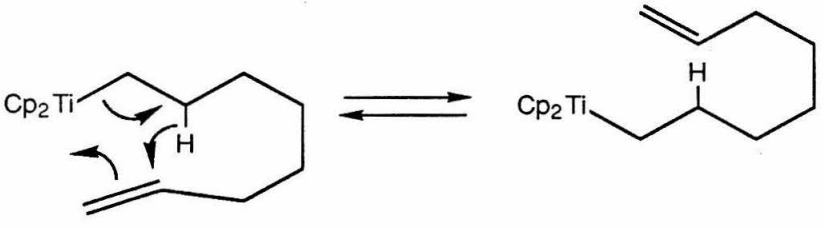


From these observations, the ideal titanium compound to compare to these other systems is titanocene ethyl chloride. In the presence of a Lewis acid co-catalyst with no olefin to compete with a β-hydrogen for the electrophilic metal center, this compound should be the one that most closely parallels the steric and electronic makeup of the aforementioned compounds. Titanocene ethyl chloride was treated with $EtAlCl_2$ in toluene-d_8 or dichloromethane-d_2 and monitored by NMR at low temperature. The only significant change in the spectrum from $Cp_2TiEtCl$ alone is a downfield shift in the signal for the α-methylene protons. At temperatures down to -100 °C, there is no indication of inequivalence in the β-hydrogens on the ethyl group. This is consistent with no β-hydrogen interaction in titanocene alkyl systems that undergo olefin insertion. The interaction could be a low-energy exchange process that cannot be observed at this temperature, but there is other evidence supporting no β-hydrogen interaction in titanocene alkyl chloride systems. It is known that $Cp_2TiEtCl$ is a better polymerization catalyst

than $Cp_2TiMeCl$, as would be expected from bond strength arguments.[27] This is in contrast with the permethylscandocene system in which the ethyl derivative reacts with ethylene more slowly than the methyl derivative. β-Hydrogen interaction has been invoked to account for this behavior.

Chain Transfer

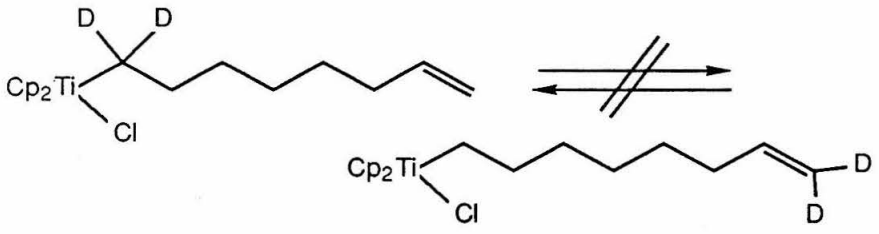
It is known that titanocene octenyl chloride **8a** does not undergo olefin insertion upon treatment with a Lewis acid. The entropy term involved in forming a seven-membered ring is presumably too large for the reaction to proceed. It was thought that since this compound does not undergo the expected lowest energy process, olefin insertion, other processes might be observed. Upon treatment with a Lewis acid, this "nonpolymerizable" pendant olefin might react with the metal center to effect a "chain transfer" *via* a retro-ene reaction. This process would presumably have a more favorable transition state than the seven-membered ring formed in olefin insertion. (See Equation 12.) This would be an intramolecular version of the mechanism proposed by Henrici-Olivé and Olivé for olefin-induced chain transfer.[17]



(12)

This rearrangement would, however, be a degenerate one. Therefore, in order to assay for this chain transfer type rearrangement, **8a**-α-d_2 was prepared. With this labelling, the postulated reaction could be easily determined with ^2H NMR analysis by the appearance of a signal for deuterium incorporation in the olefin

region of the spectrum. (See Equation 13.) Compound **8a**-α-d_2 was treated with three equivalents of Me_2AlCl at -30 °C for six hours. This produced no change in either the ^2H or ^1H NMR spectrum. The same results were observed with $EtAlCl_2$ at -100 °C.



(13)

SUMMARY

Fundamental processes that are involved in Ziegler–Natta polymerization have been investigated in a homogeneous Ti/Al-based model system. The most significant aspect of this model system is that it allows the direct observation of the key step in Ziegler–Natta polymerization, olefin insertion, under conditions that will effect polymerization. The titanocene alkenyl chlorides and alkyl aluminum cocatalysts provide a well-defined system to observe to a single monomer addition and primary insertion products without subsequent insertion/polymerization.

By the use of deuterium-labelled compounds, the potential interaction of the electrophilic metal center with hydrogens on the α- and β-carbons *via* 3-center, 2-electron bonds. The lack of α-hydrogen interaction provides more support for the Cossee–Arlman mechanism of direct insertion in this system. Although catalyst systems for Ziegler–Natta polymerization and olefin metathesis appear similar, the two processes are quite different. Olefin metathesis involves chemistry of titanium–carbon double bonds, while Ziegler–Natta polymerization involves that of titanium–carbon single bonds. From previous reports on β-hydrogen interaction, it appears that such an interaction is a good indication of a compound's capacity for olefin insertion. However, our findings demonstrate that it is not a general phenomenon for systems that catalyze olefin insertion.

In addition to olefin insertion, the reverse process, β-alkyl elimination, has also been examined. In this system, the driving force for the reaction is the release of ring strain. It proceeds irreversibly without competing β-hydrogen elimination.

EXPERIMENTAL SECTION

General Considerations. All manipulations of air- and/or water-sensitive compounds were performed using standard high-vacuum or Schlenk techniques. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). Compounds were transferred and stored in a nitrogen-filled Vacuum Atmospheres glovebox, equipped with an MO-40-1 purification train, DK-3E Dri-Kool conditioner, and Dri-Cold freezer. Flash chromatography was performed by the procedure of Still[28] using Woelm 32-63 (32-63 μm). Thin-layer chromatography was performed on EM Reagents 0.25 mm silica gel 60-F plates and visualized with either iodine vapor or phosphomolybdic acid/ethanol spray. All reaction temperatures were measured externally.

Materials. Toluene, diethylether, and tetrahydrofuran were stirred over CaH_2, then transferred to purple sodium-benzophenone ketyl. Pentane and hexane were stirred over concentrated H_2SO_4, washed with H_2O, dried over CaH_2, then transferred to purple sodium-benzophenone ketyl with tetraglyme. Dichloromethane was stirred over P_2O_5 or CaH_2 and degassed by evacuation of freeze-pump-thaw cycles. Dried degassed solvents were vacuum-transferred into dry glass vessels equipped with Teflon valve closures and stored under argon. Benzene-d_6, toluene-d_8, and tetrahydrofuran-d_8 (Cambridge Isotopes) were dried and vacuum-transferred from purple sodium-benzophenone ketyl. Chloroform-d (Aldrich) was dried over 4 Å molecular sieves. Dichloromethane-d_2 (Cambridge Isotopes and Norell, Inc.) was dried over CaH_2 and degassed by several freeze-pump-thaw cycles. Titanocene dichloride and zirconocene dichloride was obtained from Boulder Scientific. Zirconocene hydridochloride[29] was prepared by Doug Meinhart. Ethylene was obtained from Matheson and used as received. $EtAlCl_2$ and Me_2AlCl were obtained from Alfa and purified by sublimation and distillation, respectively.

Anhydrous tert-butylhydroperoxide, $Eu(fod)_3$, and all other chemicals not otherwise specified were obtained from Aldrich.

1-Chloro-5-hexene was purchased from Wiley Organics and distilled before use. 1-Chloro-6-heptene was prepared by a BH_3·THF reduction of 6-heptenoic acid (aldrich) followed by treatment with thionyl chloride. 1-chloro-5-hexene-1-d_1 and 1-chloro-6-heptene-1-d_1 were prepared by oxidation of the corresponding alcohol with pyridinium chlorochromate followed by $LiAlD_4$ reduction and treatment with thionyl chloride. Cyclobutylmethyl chloride was prepared from cyclobutylmethanol (Aldrich). $MeO_2C(CH_2)_5CHO$ was prepared from cycloheptene by the method of Schreiber.[30] This compound was used to prepare 1-chloro-7-octene and 1-chloro-7-octene-1-d_2; the ester–aldehyde was treated with methylene triphenylphosphorane, reduced with $LiAlH_4$ ($LiAlD_4$), and treated with thionyl chloride. 1-chloro-4-pentene-1-d_2 was prepared by $LiAlD_4$ reduction of ethyl 4-pentenoate (Wiley Organics). 1-chloro-5-hexene-2-d_1 was prepared by deuterozirconation of 1,5-hexadiene (Wiley Organics) with Cp_2ZrDCl, followed by treatment with N-chlorosuccinimide.[31]

Instrumentation. NMR spectra were recorded on a Varian EM-390 (90 MHz, ^1H), JEOL FX-90Q (89.60 MHz, ^1H; 22.53 MHz, ^{13}C), JEOL GX-400 (399.65 MHz, ^1H; 100.4 MHz, ^{13}C, 61.37 MHz, ^2H) or Brüker WM-500 (500.13 MHz, ^1H, 77.6 MHz, ^2H). Chemical shifts are reported in δ, referenced to residual solvent signals (^1H: C_6D_6, δ 7.15; C_7D_8, δ 2.09; THF-d_8, δ 3.58 or 1.73; CD_2Cl_2, δ 5.32; $CDCl_3$, δ 7.24; ^{13}C: C_6D_6, δ 128.0; C_7D_8, δ 20.9; THF-d_8, δ 67.4; $CDCl_3$, δ 77.0). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), coupling constant (Hz), integration and assignment. Gas chromatography analyses were performed on a Shimadzu GC-Mini-2 equipped with an SE-30 capillary column, flame-ionization detector, and a Hewlett-Packard 3390A integrator.

Sample preparation for low-temperature NMR experiments

The titanocene compound was loaded into a tared NMR tube in the drybox. Toluene-d_8, or CD_2Cl_2 (350-400 μL) was added to the tube. A latex septum was fitted onto the tube, and it was sealed with Parafilm. The standardized C_6D_6 solution of Me_2AlCl and internal standard (mesitylene or 1,2-dichloroethane) were added *via* gastight syringe. (The Me_2AlCl solution was kept frozen between uses and titrated regularly.) The tube was shaken briefly and placed in the precooled NMR probe.

Preparation of titanocene alkenyl (alkyl) chlorides

A solution of Cp_2TiCl_2 in 35 mL of CH_2Cl_2 was cooled to -30 °C. To this was added a ca. 1.0 M solution of the appropriate Grignard reagent in THF. The addition was accompanied by a rapid color change from red-orange to dark red. After 15 min the cooling bath was removed, and the reaction mixture was allowed to stir at room temperature for 2 h. The solvent was removed *in vacuo*, and the brick red solid was taken up in hexane, stirred and cannula-transferred to serum-capped, nitrogen-filled centrifuge tubes. The solution was centrifuged, and the red supernate was cannula-decanted into a Schlenk flask and crystallized at -50 °C. Yields generally ranged from 40-60%.

5a: ^{1}H NMR (400 MHz, C_6D_6): δ 5.7-6.0 (m under Cp peak, 1H) 5.80 (s, 10H), 5.15 (dd, J=6.1 Hz, 1.0 Hz, 1H), 4.95 (d, J=1.0 Hz, 1H), 1.83-1.97 (m, 2H), 1.45-1.63 (m, 4H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 139.7, 115.6, 114.9, 39.3, 36.9, 30.4.

5a-α-d_2: ^{1}H NMR (400 MHz, C_6D_6): δ 5.7-6.0 (m under Cp peak, 1H) 5.80 (s, 10H), 5.13 (dd, J=6.1 Hz, 1.0 Hz, 1H), 4.95 (d, J=1.0 Hz, 1H), 1.83-1.97 (m, 2H), 1.45-1.53 (m, 2H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 139.3, 115.9, 114.5, 39.6, 37.2. ^{2}H NMR (61.37 MHz, C_6D_6): δ 1.50 (br s).

5b: ^{1}H NMR (400 MHz, C_6D_6): δ 5.81 (s, 10H), 4.81-5.08 (m, 2H), 1.82-1.91 (m, 2H), 1.63-1.79 (m, 2H), 1.59 (d, J=6.8 Hz, 2H) 1.45-1.58, (m, 2H); ^{13}C NMR (400 MHz, C_6D_6): δ 115.5, 81.3, 45.3, 35.0, 18.3.

6a: ^{1}H NMR (400 MHz, C_6D_6): δ 5.6-6.0 (m under Cp peak, 1H), 5.78 (s, 10H), 5.12 (dd, J=6.0 Hz, 1.0 Hz, 1H), 4.97 (d, J=1.0 Hz, 1H), 2.01 (q, J_{obsd}=6.0 Hz, 2H), 1.52 (br s, 2H), 1.03-1.81 (m, 4H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 139.6, 115.6, 114.4, 72.1, 37.2, 34.5, 33.7.

6a-α-d_1: ^{1}H NMR (90 MHz, C_6D_6): δ 5.6-6.0 (m under Cp peak, 1H), 5.78 (s, 10H), 5.12 (dd, J=6.0 Hz, 1.0 Hz, 1H), 4.98 (d, J=1.0 Hz, 1H), 2.04 (q, J=6.0 Hz, 2H), 1.48 (br s, 1H), 1.05-1.90 (m, 4H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 140.1, 115.5, 114.6, 72.3, 37.5, 34.0, 33.1; ^{2}H NMR (61.37 MHz, C_6D_6): δ 1.54 (br s).

6a-β-d_1: ^{1}H NMR (90 MHz, C_6D_6): δ 5.6-6.0 (m under Cp peak, 1H), 5.78 (s, 10H), 5.14 (dd, J=6.0 Hz, 1.0 Hz, 1H), 5.00 (d, J=1.0 Hz, 1H), 2.04 (q, J=6.0 Hz, 2H), 1.51 (br s, 2H), 1.08-1.89 (m, 3H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 140.1, 115.5, 114.6, 72.3, 37.5, 34.0, 33.1; ^{2}H NMR (61.37 MHz, C_6D_6): δ 1.40 (br s).

6b: ^{1}H NMR (90 MHz, C_6D_6): δ 5.81 (s, 10H), 1.3-1.7 (m, 11H); ^{13}C NMR (90 MHz, gated decoupled, C_6D_6): δ 115.5 (d, $^1J_{CH}$=174 Hz), 82.5 (t, $^1J_{CH}$=125 Hz), 48.3 (d, $^1J_{CH}$=127 Hz), 37.2 (t, $^1J_{CH}$=132 Hz), 25.3 (t, $^1J_{CH}$=126 Hz).

6b-α-d_1: ^{2}H NMR (78 MHz, tol-d_8): δ 0.62, 1.73.

6b-β-d_1: ^{2}H NMR (78 MHz, tol-d_8): δ 1.46, 1.57.

7a: ^{1}H NMR (400 MHz, C_6D_6): δ 5.6-6.0 (m, under Cp peak, 1H), 5.78 (s, 10H), 5.14 (dd, J=6.0 Hz, 1.0 Hz, 1H), 4.93 (d, J=1.0 Hz, 1H), 2.04 (q, J=6.0 Hz, 2H) 1.57 (br s, 2H), 1.05-1.93 (m, 6H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 140.0, 115.7, 114.8, 72.8, 37.2, 34.9, 33.4, 29.3.

7a-α-d_1: ^{1}H NMR (400 MHz, C_6D_6): δ 5.6-6.0 (m, under Cp peak, 1H), 5.78 (s, 10H), 5.14 (dd, J=6.0 Hz, 1.0 Hz, 1H), 4.93 (d, J=1.0 Hz, 1H), 2.08 (q, J=6.0

Hz, 2H), 1.52 (br s, 1H), 1.09-1.90 (m, 6H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 139.6, 115.6, 114.0, 72.6, 37.9, 35.2, 33.9, 30.1.

7b: ^{1}H NMR (400 MHz, C_6D_6): δ 5.81 (s, 10H), 1.32-1.69 (m, 13H); ^{13}C NMR (90 MHz, gated decoupled, C_6D_6): δ 115.5 (d, $^1J_{CH}$=174 Hz), 82.5 (t, $^1J_{CH}$=125 Hz), 48.3 (d, $^1J_{CH}$=127 Hz), 37.2 (t, $^1J_{CH}$=132 Hz), 25.3 (t, $^1J_{CH}$=126 Hz).

8a: ^{1}H NMR (90 MHz, C_6D_6): δ 5.7-6.0 (m, under Cp peak, 1H), 5.78 (s, 10H), 5.12 (dd, J=6.1 Hz, 1.2 Hz, 1H), 4.96 (d, J=1.2 Hz, 1H), 2.01 (q, J=6.1 Hz, 2H), 1.55 (br s, 2H), 0.98-1.91 (m, 8H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 139.5, 115.4, 114.5, 72.3, 38.1, 35.0, 33.7, 29.3, 28.5.

8a-α-d_2: ^{1}H NMR (90 MHz, C_6D_6): δ 5.7-6.0 (m, under Cp peak, 1H), 5.78 (s, 10H), 5.14 (dd, J=6.2 Hz, 1.1 Hz, 1H), 4.95 (d, J=1.1 Hz, 1H), 2.10 (q, J=6.0 Hz, 2H), 0.94-1.89 (m, 8H); ^{13}C NMR (22.53 Mz, C_6D_6): δ 140.2, 115.2, 114.3, 71.9, 37.0, 35.8, 33.2, 29.4.

Ethylene oligomerization

$EtAlCl_2$ cocatalyst. Separate solutions of **6a** (40 mg) and $EtAlCl_2$ (125 mg) were prepared in 2 mL of toluene (or dichloromethane). The two solutions were degassed by three cycles of freeze-pump-thaw at −196 °C. The solution of **6a** was stirred under an atmosphere of ethylene at −100 °C for 45-60 min. The $EtAlCl_2$ solution was prepared likewise at −30 °C. The $EtAlCl_2$ solution was quickly added to the rapidly stirring solution of **6a** *via* cannula. After 10 sec, the oligomerization was quenched with HCl/MeOH.

Me_2AlCl cocatalyst. The oligomerization was performed as above, except that both solutions were stirred at −30 °C under ethylene.

Preparation of Cp_2ZrDCl

A solution of Cp_2ZrCl_2 (11.0 g, 37.6 mmol) was prepared in 100 mL of THF. To this was added a suspension of $LiAlD_4$ (418 mg, 9.95 mmol) in 40 mL of THF over a period of 10 min. The reaction mixture was allowed to stir at room temperature for 3 h. The heterogeneous mixture was filtered through a coarse Schlenk frit. The white powder was washed with THF (3 × 10 mL) and held *in vacuo* overnight to yield 7.3 g (75%). The product was analyzed for purity as described by Schwartz[31] and found to be 80% pure.

Preparation of diastereomeric alcohols

A solution of 50 mg (0.168 mmol) of **6a**-β-d_1 in 2 mL of toluene was cooled to −50 °C. To this was added 2 equiv of Me_2AlCl in 0.5 mL of toluene. The reaction mixture was allowed to stir at −50 °C for 1 h. An excess of pyridine was added, and the reaction mixture was allowed to warm to room temperature. The solvent was removed *in vacuo*. The red solid was redissolved in toluene. To this was added a two molar excess of anhydrous TBHP (3.0 M in toluene). The reaction mixture was allowed to stir at room temperature overnight. The volatiles were vacuum-transferred, and the diastereomeric alcohols were analyzed by ^2H NMR. Without $Eu(fod)_3$, there were two unresolved signals at 1.44 and 1.60 ppm. With $Eu(fod)_3$, the signals shifted to 1.51 and 1.85 ppm, and the ratio of the peak areas was 0.98 ± 0.05.

2-Butyne trapping experiments

A toluene (or dichloromethane) solution of the titanocene (or zirconocene) cyclobutylmethyl chloride was cooled to −30 °C. To this was added a 10-fold excess of 2-butyne. This was folowed by the addition of a toluene solution of Me_2AlCl (2-5 equiv). After stirring at −30 °C for 1 h, pyridine (2-5 equiv) was

added. The reaction mixture was warmed to room temperature, and the solvent and excess 2-butyne were removed *in vacuo*. The reaction with **5b** gave only the β-alkyl elimination product **5a**. The insertion of 2-butyne into a Ti–alkyl bond is very slow at this temperature. The reaction with Zr produced only the product from hydride trapping by 2-butyne **9**.

5b(Zr): ^{1}H NMR (400 MHz, CD_2Cl_2): δ 6.22 (s, 10H), 2.00-2.11 (m, 1H), 1.60-1.69 (m, 2H), 1.43-1.49 (m, 2H), 1.19 (d, J=7.3, 2H).

6a(Zr): ^{1}H NMR (400 MHz, CD_2Cl_2): δ 6.27 (s, 10H), 5.18-5.37 (m, 1H), 4.91-5.13 (m, 2H), 2.10 (q, J=6.0 Hz, 2H), 1.37 (m, 6H).

9: ^{1}H NMR (400 MHz, CD_2Cl_2): δ 6.18 (s, 10H), 5.83 (br t, J=6.0 Hz, 1H), 2.69 (d, J=6.0 Hz, 3H), 2.01 (d, J=6.0 Hz, 3H).

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19. Unless otherwise stated, all experiments described herein were conducted with both of these Lewis acids. All NMR experiments were performed with Me_2AlCl. Line broadening caused by $EtAlCl_2$ precluded its use in NMR work.

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22. The ring strain in cyclobutane is 26.2 kcal/mol.[20]

23. For further discussion, see Chapter 5 of this thesis.

24. The same reactivity is observed in the absence of a Lewis acid.

25. For a discussion, see Soto, J.; Steigerwald, M.; Grubbs, R. H. *J. Am. Chem. Soc.*, **1982**, *104*, 4479.

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Chapter 5

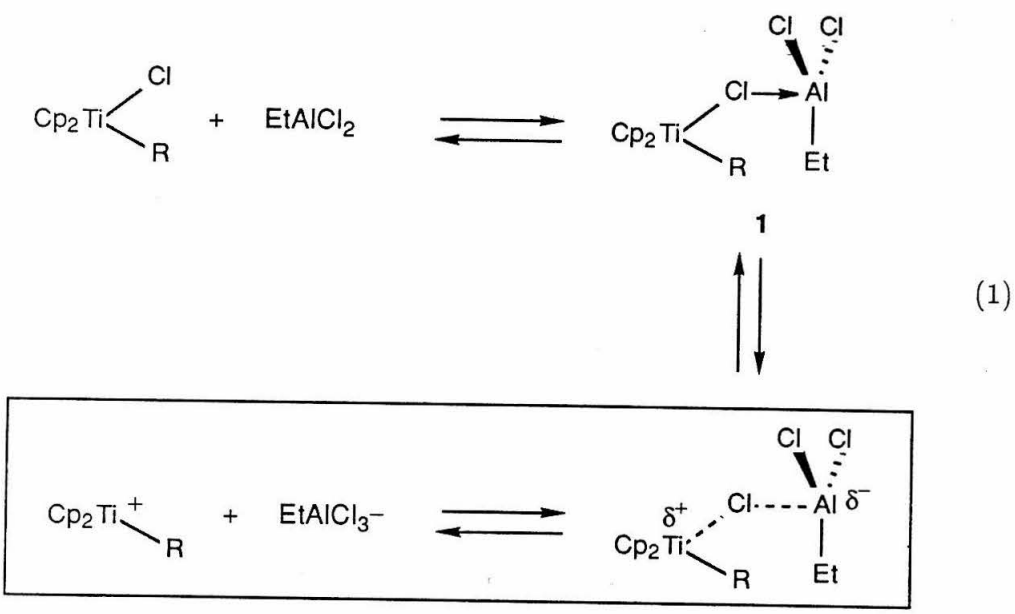
Studies on the Chemical Nature of the Active Species in a Soluble Ziegler–Natta Polymerization System

INTRODUCTION

The mechanism of olefin polymerization by homogeneous Ziegler–Natta catalysts has been the object of continuous study for over 25 years.[1] In Chapter 4, we described the use of a homogeneous Ti/Al model system to investigate some of the elementary steps in this process. In this chapter, we will use similar compounds in an attempt to probe the nature of the interaction of the titanocene compounds with the alkyl aluminum and other potential cocatalysts. These studies are directed toward exploring the chemical nature of the active site, the particular species that reacts with a monomer unit before its addition to the growing polymer chain. The identity of this complex remains a matter of controversy. Although it is now widely accepted that the transition metal, not the main group cocatalyst, is the location of the addition of the monomer to the growing polymer chain, a more specific description of this site remains elusive.

As early as 1959, Breslow and co-workers[2] proposed that the active species in $Cp_2TiCl_2/AlR_nCl_{(3-n)}$ model systems is a titanium–aluminum alkyl complex **1** or a species derived therefrom. (See Equation 1.) This hypothesis was based on chemical and UV-vis spectroscopic studies. The proposed role of the aluminum cocatalyst is two-fold. Its first function is to alkylate Cp_2TiCl_2. The resulting aluminum species then activates Cp_2TiRCl by Lewis acid complexation with, or complete removal of, the chlorine ligand. Polymerization is proposed to involve coordination of the olefin prior to its insertion into the Ti–R bond. The notion of direct insertion into a transition-metal–alkyl bond is the Cossee–Arlman mechanism.[3]

Early in the study of this reaction, it was thought that activation involved more than simple complex formation. It was postulated that extrusion of $[AlR_{(n-1)}Cl_{(5-n)}]^-$ to form a titanium cation, the presumed active species, was necessary. The first supporting evidence for a cationic active site came from

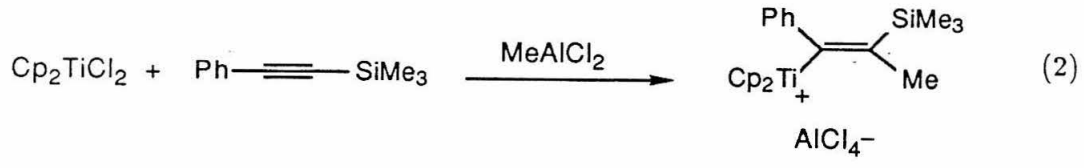


(1)

Dyachkovskii and co-workers.[4] In a series of experiments employing solvents of different polarity, titanium cations could be detected by electrodialysis. Ethylene polymerization was observed in the cathode chamber, commencing upon migration of the titanium cations from the anode to the cathode chamber.

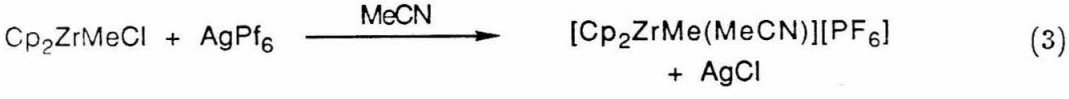
One system examined by Eisch and co-workers[5] is similar to the typical homogeneous Ti/Al systems used for many years. In this study, a highly substituted alkyne, trimethyl(phenylethynyl)silane, was used as an "ethylene surrogate" in the insertion process. (See Equation 2.) In this reaction, the cationic carbotitanation product **2** was isolated. While this result is consistent with the intermediacy of a cationic species, it does not prove that a cationic species is the active agent. The isolated complex is a product; the species that actually reacts with the alkyne is not observed. Furthermore, this particular cationic complex does not react with ethylene.

Jordan and co-workers[6] have taken another approach employing zirconium in

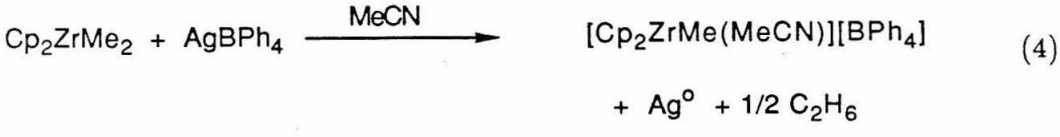


(2)

a system that contains no aluminum cocatalyst. They have prepared Cp_2ZrR^+ complexes *via* X^- or R^- abstraction from Zr(IV) by Ag^+. (See Equations 3 and 4.) These highly electrophilic compounds are isolated as solvent adducts. They exhibit behavior different from that of their neutral Zr(IV) analogues. The cationic acyl species produced by treatment with CO do not release CO under vacuum as do the neutral acyl compounds. Also, the cationic zirconium alkyls react rapidly with ketones under mild conditions. Finally, the THF adducts of these cationic complexes will polymerize ethylene in the absence of an aluminum cocatalyst. This supports the theory that the purpose of the cocatalyst (after transition-metal alkylation) is the generation of a very polarized or cationic species. It follows that such a cation, generated independently, should be able to polymerize olefins in the absence of a cocatalyst.



(3)



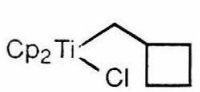
(4)

The fact that an electron-deficient, coordinatively unsaturated cationic metal alkyl would rapidly insert an olefin is not surprising. It therefore follows that

isoelectronic metal alkyls should exhibit similar reactivity. This hypothesis is supported by results reported by a number of workers. Watson[7] has found that $(C_5Me_5)_2LuCH_3$ will polymerize ethylene. The direct insertion of proplylene has also been observed with this compound. Similarly, Marks, *et. al.*[8] have prepared a series of lanthanide hydride dimers $[(C_5Me_5)_2MH]_2$ (M= La, Nd, Lu), and have shown that these complexes are highly reactive toward polymerization of ethylene. Yet another example of an early transition-metal polymerization system is one based on scandium. Permethylscandocene alkyls that are isoelectronic with titanocene alkyl cations have been reported by Bercaw and co-workers.[9] These compounds are quite reactive toward olefin insertion and polymerization.

RESULTS AND DISCUSSION

NMR spectroscopy was used to study the formation and chemical nature of Ti/Al adducts. The change in electron density at the metal center upon treatment of the titanocene compounds **3-5** with Me_2AlCl causes a shift in the NMR signals for these compounds. The most diagnostic change is in the signal for the cyclopentadienyl rings. This signal moves downfield upon association with the added Lewis acid (LA), indicating decreased electron density at the metal center. (See Figure 1.) This downfield shift continues with increasing LA concentration until approximately one equivalent has been added and all the starting titanium substrate is consumed by the formation of a 1:1 Ti/Al complex. Further addition of LA produces a a proportionately more gradual shift in signals perhaps by facilitating the formation of a further polarized species. (See Equation 1.) At amounts of less than one equivalent of Me_2AlCl, there is never more than one species observed. Even at temperatures as low as -100 °C, resolved signals for complexed and uncomplexed **4** are not observed. The slight broadening of the signal also indicates a rapid exchange.



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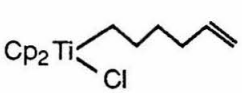

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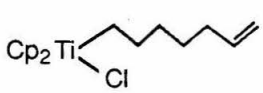


5

In a typical experiment, aliquots of a solution of Me_2AlCl are added to the titanium complex at the temperature at which the reaction is to be monitored. After each addition of Me_2AlCl, the solution is allowed to equilibrate before the position of the signal is noted. However, at higher concentrations, examination of

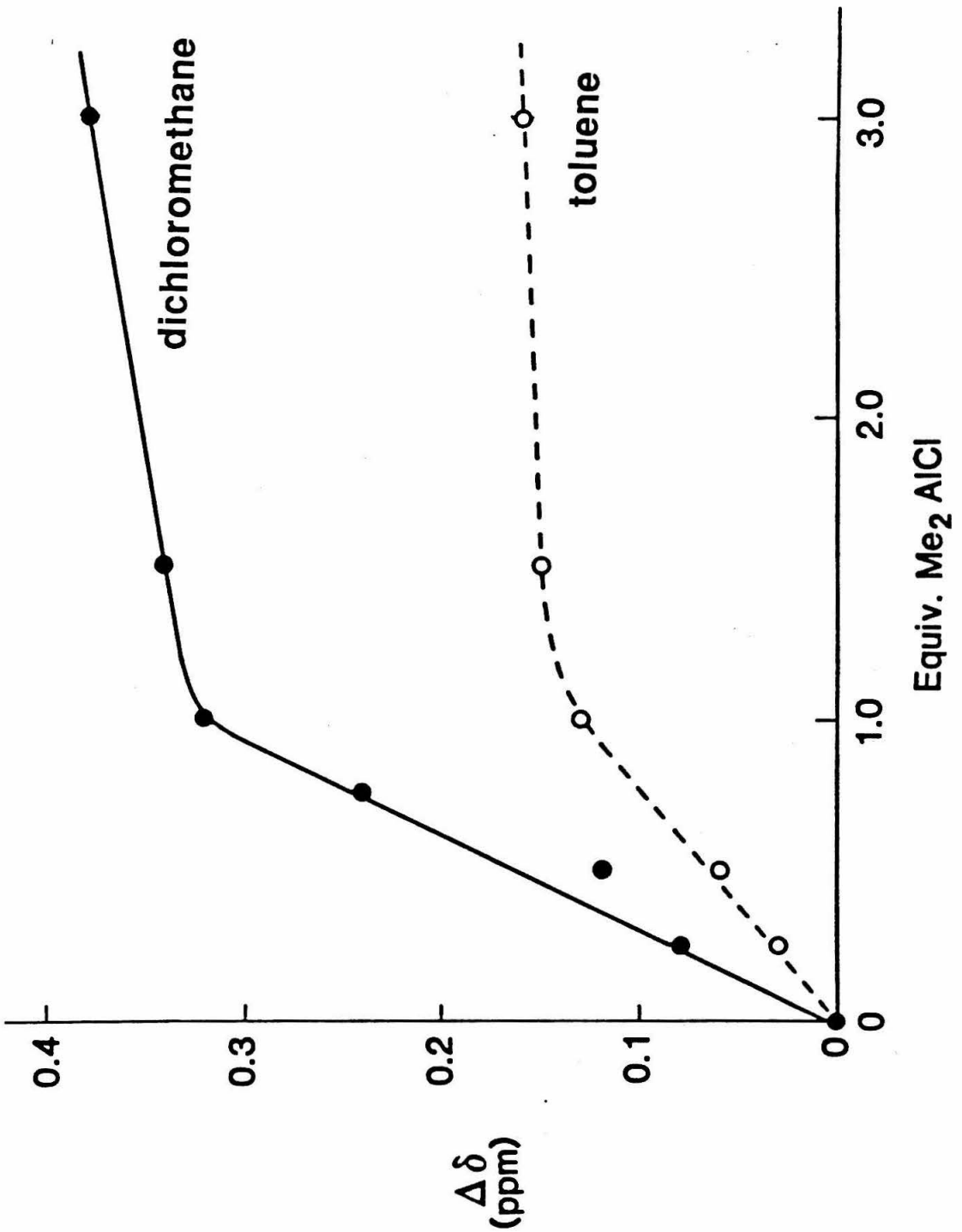
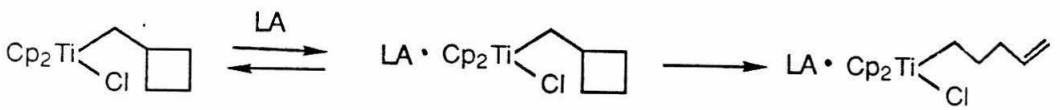


Figure 1. The shift in NMR signals of **4** as a function of Lewis acid concentration.

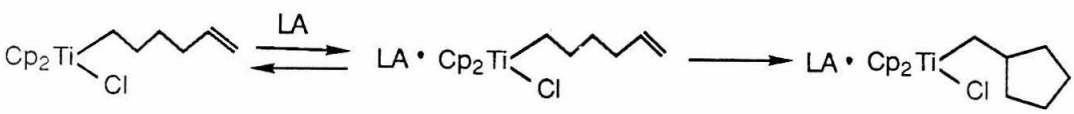
the spectrum is often complicated by the appearance of signals due to the respective reaction product. Therefore, the experiment was repeated with titanocene pentenyl chloride and titanocene cyclohexylmethyl chloride which do not undergo olefin insertion or β-alkyl elimination, respectively. The NMR spectra of these compounds show the same pattern of shifting signals for the cyclopentadienyl rings with no resolved signals for complexed and uncomplexed titanocene compounds. The polarization of the metal–carbon bond can be more dramatically seen by treating $Cp_2TiEtCl$ with Me_2AlCl in CD_2Cl_2. This produces a 0.6 ppm shift in the quartet for the α-methylene group. These results further demonstrate that the polarization of the metal–carbon bond is not induced by an incoming olefin.

Along with the chemical nature of the metal center in the transition state, the question of monomer-to-metal coordination prior to insertion remains uncertain. While it has been proposed that the monomer forms a π-complex at the metal center prior to insertion,[10] there is scant evidence supporting this hypothesis. Preliminary UV-vis spectroscopic studies on the titanocene alkenyl chlorides concluded that in solution, the pendant olefin is not coordinated to the metal center.[11] More relevant to the situation at the time of monomer addition is the interaction, if any, in the presence of an LA. In NMR studies on compounds **4** and **5**, addition of LA produces no perceptible shift in the signals for the olefin protons. The same is true in the reverse reaction, β-alkyl elimination. This reaction can be followed by treating **3** with LA and noting the appearance of the olefin signals in the NMR spectrum. When the reaction is complete, and a Lewis base is added to coordinate the LA, the olefin signals do not shift. The fact that this intramolecular olefin shows no perceptible interaction with the metal center argues strongly against olefin coordination prior to insertion. This observation is in agreement with those of other workers who report no evidence of prior monomer coordination.[12]

Just as the change in chemical shift is dependent on the amount of added LA, the rates of β-alkyl elimination and intramolecular olefin insertion are also dependent upon the concentration of LA. These reactions were studied using compounds **3** and **4**, respectively. (See Equations 5 and 6.) From repeated examination of these reactions at various concentrations of LA, it was observed that the rates are concentration dependent, but this remains a qualitative observation. The exact rates for these reactions have not been obtained. However, approximate $t_{1/2}$'s could be determined. (See Table 1.) Although the reported numbers are approximate, the trends are reproducible.



(5)



(6)

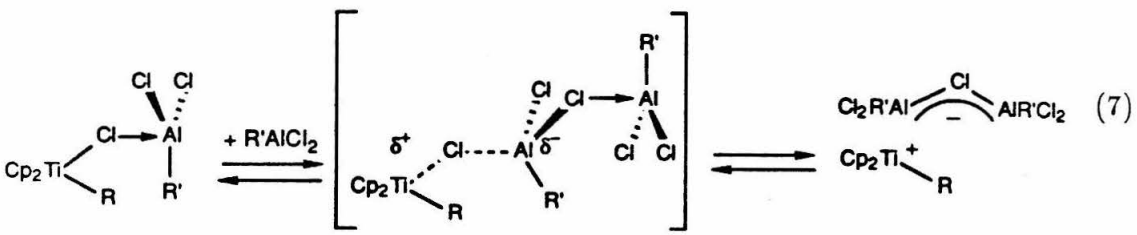
If simple complex formation were enough to induce these reactions, it would appear that these are second-order reactions in which complex formation is the rate-determining step. (See Equations 5 and 6.) However, other workers have determined that the formation of this complex is diffusion-controlled.[12] Nevertheless, the rate increases with the concentration of cocatalyst, leveling off at ca. 3-4

equivalents Me_2AlCl	$t_{1/2}$ (min)			
	3[a]	**4**[a]	**4**[b]	**4**[c]
0.25	28	17	42	21
0.50	21	12	37	12
0.75	15	7	29	6
1.00	12	5	18	5
1.50	9	3	15	4
3.00	<5	<3	10	<3

Table 1. Approximate $t_{1/2}$'s for ß-alkyl elimination and olefin insertion.

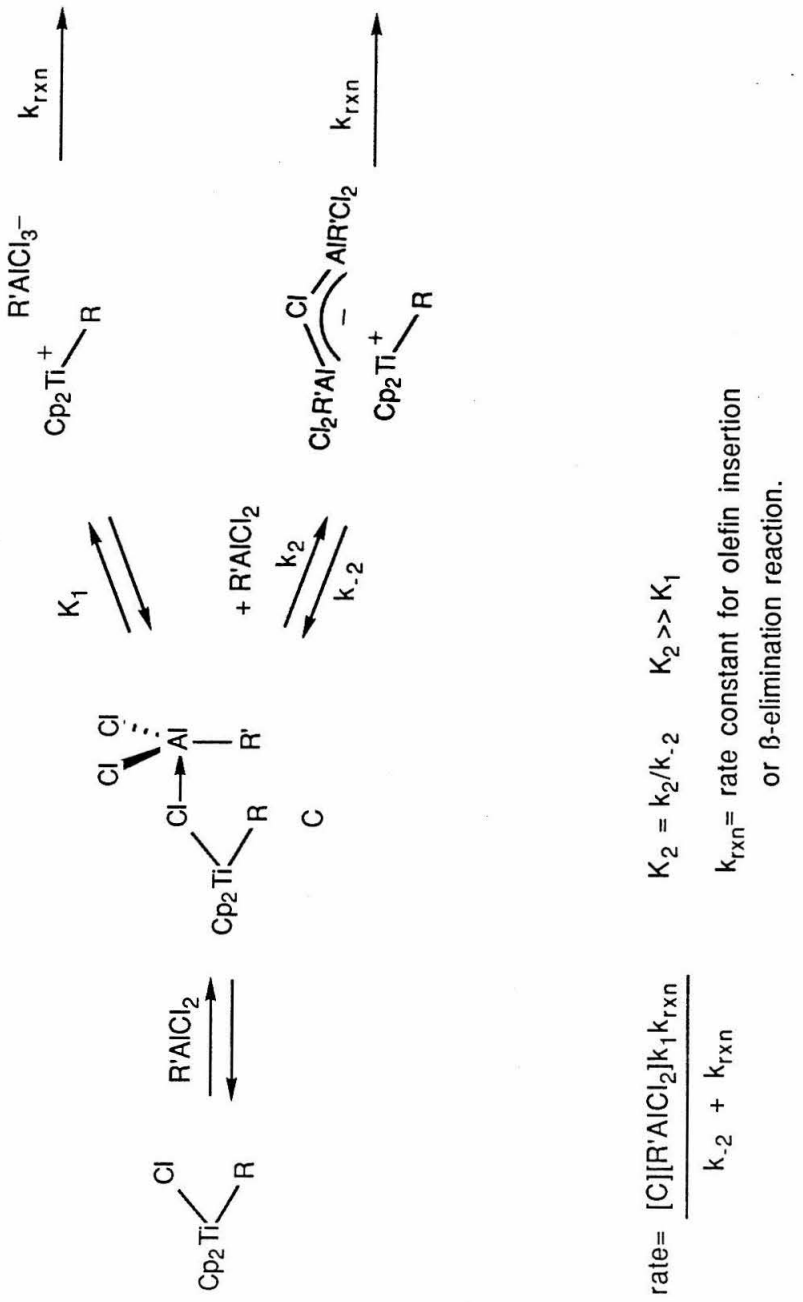
a. toluene-d_8, -35 °C
b. toluene-d_8, -50 °C
c. dichloromethane-d_2, -50 °C

equivalents.[13] This concentration dependence suggests the need for at least two equivalents of LA to effect the olefin insertion. A possible mechanism is outlined in Scheme 1. The second equivalent of LA assists the formation of the active species, pictured in this scheme as a titanium cation. (See Equation 7.) The formation of a di-aluminum species allows for delocalization of the incipient negative charge, thereby driving the equilibrium and increasing the concentration of the active species. A similar scheme has been proposed by Fink[14] in which an initial inactive 1:1 Ti/Al complex is formed prior to the formation of the active species. The supposition is that the inactive complex is then activated upon interaction with "a dimeric aluminum species of unknown nature." Our proposed mechanism is an extension of this idea. In this mechanism there could be parallel equilibria involving a single cationic titanium active species with a chlorine-linked dimeric aluminum counterion. In this system, there is no evidence to imply that a 1:1 Ti/Al adduct is *inactive*. The LA concentration dependence merely suggests that $K_2 >> K_1$. The fact that **3** and **4-5** undergo β-alkyl elimination and olefin insertion, respectively, at different rates demonstrates that the last step, k_{rxn}, is rate-determining in this model system.



(7)

We have observed that **4** and **5** undergo $EtAlCl_2$-catalyzed olefin insertion at much different rates. Although the reaction with **5** is much slower, it does proceed quantitatively with this LA cocatalyst. However, using quantities of up to five equivalents of Me_2AlCl as the LA cocatalyst, insertion is not observed with **5**.



Scheme 1. Proposed kinetic scheme for olefin insertion and β-alkyl elimination in a homogeneous Ziegler–Natta system.

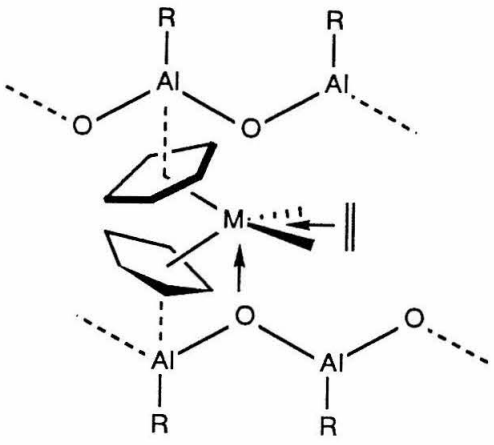


Figure 2. Proposed interaction between oligomeric aluminoxane and metallocene polymerization catalyst. (ref. 16)

When water is added to the reaction in the ratio of 5:1, LA to H_2O, insertion takes place quantitatively as with $EtAlCl_2$. The added water presumably reacts with Me_2AlCl to produce oligomeric aluminoxanes $[-Al(R)-O-]_n$. These species have recently come into use as cocatalysts in some zirconium systems.[15] These systems show great promise as high activity Ziegler–Natta polymerization systems producing polymers with relatively low molecular weight distributions. The role of aluminoxanes in the polymerization is not well understood. A common explanation invokes a hexacoordinate intermediate with an aluminoxane oxygen coordinated at the metal center through an interaction between aluminum and the cyclopentadienyl ligands.[16] (See Figure 2.) This scheme requires concomitant cyclopentadienyl reorganization to an η^3 or η^1 structure. Alternatively, a simpler, and therefore more attractive, explanation not involving any specific aluminoxane–metal interaction might account for this activity. The oligomeric aluminoxanes might surround the transition metal species and provide a polar environment that would stabilize the catalytic centers. Furthermore, the oligomeric structure could delocalize the negative charge. This hypothesis is supported by the fact that dimeric species

of the type $(R_2Al)_2O$ will not effect polymerization.[15c] Also, the activity of an aluminoxane–transition-metal catalyst system increases and the molecular weight distribution decreases as the degree of aluminoxane oligomerization increases.[15a,c] Although aluminoxanes are less Lewis acidic than alkyl aluminum chlorides, the key to their activity may lie in their ability to stabilize the catalytic species.

SUMMARY

NMR studies on the adduct formed between the titanocene alkyl chloride and the Lewis acid show a concentration-dependent decrease in electron density at the metal center. There is no evidence from the NMR spectrum for olefin coordination to the catalyst prior to the insertion. An LA concentration dependence is also seen in the olefin insertion and β-alkyl elimination reactions in the model compounds. However, because the overall reactions occur at different rates, it is thought that the last step in which olefin insertion or β-alkyl elimination occurs is rate-determining. Increased concentration of LA drives the equilibrium towards the formation of the active species. An alternate hypothesis to explain the activity of aluminoxane cocatalysts is given. This states that it is simply the polar environment provided by the oligomeric aluminoxanes rather than any specific aluminoxane–transition-metal interaction that is most important.

EXPERIMENTAL SECTION

General Considerations. All manipulations of air- and/or water-sensitive compounds were performed using standard high-vacuum or Schlenk techniques. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). Compounds were transferred and stored in a nitrogen-filled Vacuum Atmospheres glovebox, equipped with an MO-40-1 purification train, DK-3E Dri-Kool conditioner, and Dri-Cold freezer. All reaction temperatures were measured externally.

Materials. Toluene, diethylether, and tetrahydrofuran were stirred over CaH_2, then transferred to purple sodium-benzophenone ketyl. Pentane and hexane were stirred over concentrated H_2SO_4, washed with H_2O, dried over CaH_2, then transferred to purple sodium-benzophenone ketyl with tetraglyme. Dichloromethane was stirred over P_2O_5 or CaH_2 and degassed by evacuation of freeze-pump-thaw cycles. Dried degassed solvents were vacuum-transferred into dry glass vessels equipped with Teflon valve closures and stored under argon. Benzene-d_6, toluene-d_8, and tetrahydrofuran-d_8 (Cambridge Isotopes) were dried and vacuum-transferred from purple sodium-benzophenone ketyl. Chloroform-d (Aldrich) was dried over 4 Å molecular sieves. Dichloromethane-d_2 (Cambridge Isotopes and Norell, Inc.) was dried over CaH_2 and degassed by several freeze-pump-thaw cycles. Titanocene dichloride was obtained from Boulder Scientific. Titanocene alkyl chlorides were prepared as described in Chapter 4. $EtAlCl_2$ and Me_2AlCl were obtained from Alfa and purified by sublimation and distillation, respectively.

Instrumentation. NMR spectra were recorded on a Varian EM-390 (90 MHz, ^1H), JEOL FX-90Q (89.60 MHz, ^1H; 22.53 MHz, ^{13}C), JEOL GX-400 (399.65 MHz, ^1H; 100.4 MHz, ^{13}C, 61.37 MHz, ^2H), or Brüker WM-500 (500.13 MHz, ^1H, 77.6 MHz, ^2H). Chemical shifts are reported in δ, referenced to residual solvent signals (^1H: C_6D_6, δ 7.15; C_7D_8, δ 2.09; THF-d_8, δ 3.58 or 1.73;

CD_2Cl_2, δ 5.32; $CDCl_3$, δ 7.24; ^{13}C: C_6D_6, δ 128.0; C_7D_8, δ 20.9; THF-d_8, δ 67.4; $CDCl_3$, δ 77.0). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), coupling constant (Hz), integration and assignment. Gas chromatography analyses were performed on a Shimadzu GC-Mini-2 equipped with an SE-30 capillary column, flame-ionization detector, and a Hewlett-Packard 3390A integrator.

Sample preparation for NMR experiments

The titanocene compound was loaded into a tared NMR tube in the drybox. Toluene-d_8, or CD_2Cl_2 (350-400 μL) was added to the tube. A latex septum was fitted onto the tube, and it was sealed with Parafilm. The standardized C_6D_6 solution of Me_2AlCl and internal standard (mesitylene or 1,2-dichloroethane) were added *via* gastight syringe. (The Me_2AlCl solution was kept frozen between uses and titrated regularly.) The tube was shaken briefly and placed in the precooled NMR probe. The sample was allowed to equilibrate before the spectrum was recorded. When more than one aliquot of the Me_2AlCl solution was added, the sample tube was kept at -78 °C while it was out of the NMR probe.

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13. At higher LA concentrations, other reactions such as reduction complicate the reaction scheme, making it difficult to determine if there is a further concentration dependence.

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Appendix

Crystal Structure Determination

A crystal of **6** (see Chapter 3) was grown by a slow cooling of a toluene-dichloromethane solution to −50 °C. The crystal was mounted in a glass capillary tube at ambient temperature. Data were collected on a locally modified Syntex $P2_1$ diffractometer with graphite monochromator and Mo Kα radiation (λ = 0.7107 Å) to $2\theta = 50°(+h, \pm k, \pm \ell)$. The averaged data (2762) were corrected for Lorentz and polarization effects, but not for absorption (μ = 6.66 cm^{-1}). The Ti atom position was derived from the Patterson map, the remainder of the structure was located through subsequent structure factor calculations and Fourier maps. Hydrogen atoms were placed in calculated positions, assuming idealized geometry with fixed isotropic B's = 5.0 $Å^2$. Least-squares refinement of all non-hydrogen atoms with anisotropic Gaussian amplitudes resulted in R = 0.161 for the 2236 reflections with $F_o^2 > 0$, $R_{3\sigma}$ = 0.067 for 954 reflections with $F_o^2 > 3\sigma(F^2)$, and GOF = 1.29. A summary of the data collection information is given in Table 1.

Table 1. Summary of Crystal Structure Data

Fomula	$TiC_{18}H_{17}NS$
Space group	C2/c
V	3100(10) Å^3
a	30.261(20) Å
b	7.988(9) Å
c	13.512(14) Å
β	108.35(7)°
Z	8
λ	0.7107 Å
μ	6.66 cm^{-1}
Reflections	+h, ±k, ±ℓ
Collected	954

Table 2. Bond lengths (Å).

Bond	Length	Bond	Length
Ti–S	2.406(2)	Ti–N	2.032(6)
S–C(8)	1.721(8)	N–C(1)	1.400(10)
N–C(3)	1.396(9)	C(1)–C(2)	1.334(12)
C(3)–C(4)	1.404(11)	C(3)–C(8)	1.439(10)
C(4)–C(5)	1.363(13)	C(5)–C(6)	1.372(14)
C(6)–C(7)	1.383(13)	C(7)–C(8)	1.401(11)
Cp(1)–Cp(2)	1.354(14)	Cp(1)–Cp(5)	1.398(14)
Cp(2)–Cp(3)	1.379(15)	Cp(3)–Cp(4)	1.359(16)
Cp(4)–Cp(5)	1.375(15)	Cp(6)–Cp(7)	1.378(15)
Cp(6)–Cp(10)	1.343(16)	Cp(7)–Cp(8)	1.393(13)
Cp(8)–Cp(9)	1.403(12)	Cp(9)–Cp(10)	1.385(14)

Table 3. Bond angles (°).

Bonds	Angle	Bonds	Angle
N–Ti–S	82.2(2)	Ti–S–C(8)	91.2(3)
Ti–N–C(1)	129.9(5)	Ti–N–C(3)	112.8(4)
C(2)–C(1)–N	129.1(8)	C(3)–N–C(1)	116.4(6)
C(8)–C(3)–N	116.7(6)	C(4)–C(3)–N	124.1(7)
C(7)–C(8)–C(3)	118.9(7)	C(8)–C(3)–C(4)	119.1(7)
C(5)–C(4)–C(3)	119.6(8)	C(6)–C(5)–C(4)	122.0(9)
C(7)–C(6)–C(5)	120.6(9)	C(8)–C(7)–C(6)	119.8(8)
C(3)–C(8)–S	119.6(6)	C(7)–C(8)–S	121.4(6)
Cp(5)–Cp(1)–Cp(2)	108.1(9)	Cp(3)–Cp(2)–Cp(1)	108.1(9)
Cp(4)–Cp(3)–Cp(2)	108.4(10)	Cp(5)–Cp(4)–Cp(3)	108.4(10)
Cp(4)–Cp(5)–Cp(1)	107.0(9)	Cp(10)–Cp(6)–Cp(7)	107.9(10)
Cp(8)–Cp(7)–Cp(6)	108.4(9)	Cp(9)–Cp(8)–Cp(7)	107.1(8)
Cp(10)–Cp(9)–Cp(8)	106.2(8)	Cp(9)–Cp(10)–Cp(6)	110.5(10)

Table 4. Atomic Coordinates and equivalent isotropic U's ($\times$ 10^4).

Atom	x	y	z	U_{eq}
Ti	1576(1)	651(2)	2899(1)	432(3)
S	1796(1)	2354(3)	4446(1)	541(6)
N	1041(2)	23(7)	3430(4)	391(16)
C(1)	766(3)	−1424(10)	3256(6)	586(23)
C(2)	664(3)	−2475(11)	2449(6)	923(31)
C(3)	885(3)	1366(9)	3893(5)	440(23)
C(4)	423(3)	1570(11)	3884(6)	695(26)
C(5)	301(3)	2969(13)	4313(7)	903(33)
C(6)	616(4)	4204(12)	4753(6)	836(30)
C(7)	1076(3)	4059(10)	4785(5)	608(25)
C(8)	1221(2)	2643(10)	4360(5)	469(21)
Cp(1)	2152(4)	−858(13)	2434(7)	706(28)
Cp(2)	1835(3)	−1995(12)	2524(8)	794(34)
Cp(3)	1854(4)	−2062(13)	3556(10)	880(34)
Cp(4)	2185(4)	−969(15)	4104(7)	856(37)
Cp(5)	2371(3)	−182(10)	3421(10)	768(32)
Cp(6)	1058(4)	2870(16)	2002(8)	894(35)
Cp(7)	968(3)	1470(12)	1375(7)	716(32)
Cp(8)	1359(4)	1125(10)	1078(5)	618(29)
Cp(9)	1694(3)	2343(13)	1545(6)	614(25)
Cp(10))	1492(5)	3384(10)	2099(7)	876(50)

Table 5. Anisotropic Thermal Parameters ($\times 10^4$).

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Ti	527(9)	400(8)	391(8)	73(8)	178(7)	16(8)
S	585(15)	581(15)	440(12)	−30(13)	139(10)	−83(12)
N	455(40)	351(38)	331(35)	−21(33)	72(32)	−23(30)
C(1)	603(62)	602(61)	684(61)	19(49)	388(53)	−19(49)
C(2)	1077(75)	707(67)	792(66)	285(60)	17(59)	−207(59)
C(3)	418(55)	578(58)	272(40)	72(47)	34(39)	−2(40)
C(4)	701(69)	779(69)	625(58)	3(54)	239(51)	−217(51)
C(5)	617(68)	1189(97)	1024(80)	11(63)	431(61)	−527(69)
C(6)	973(82)	858(76)	654(62)	358(70)	224(61)	−229(61)
C(7)	758(65)	502(61)	540(52)	98(54)	168(49)	−131(48)
C(8)	472(54)	556(57)	355(42)	90(47)	95(39)	32(43)
Cp(1)	869(78)	792(76)	559(61)	454(63)	371(60)	109(62)
Cp(2)	647(72)	634(77)	1019(86)	80(56)	146(66)	−223(66)
Cp(3)	980(91)	907(94)	977(89)	541(70)	627(76)	508(74)
Cp(4)	894(89)	1046(104)	602(70)	545(75)	197(64)	24(69)
Cp(5)	586(65)	601(69)	1012(82)	166(50)	100(66)	−68(63)
Cp(6)	1091(96)	1061(101)	726(74)	561(82)	566(76)	313(68)
Cp(7)	480(66)	916(83)	636(65)	106(58)	9(54)	360(57)
Cp(8)	1003(76)	610(70)	279(43)	156(59)	255(49)	56(42)
Cp(9)	584(60)	669(65)	537(54)	−161(56)	103(48)	172(51)
Cp(10)	1889(123)	221(52)	481(56)	268(72)	320(78)	37(44)

Table 6. Hydrogen atom coordinates ($\times 10^4$) and B's ($\times 10^3$).

Atom	x	y	z	B
H(1)	634	−1697	3788	5.0
H(2A)	498	−2085	1769	5.0
H(2B)	756	−3616	2553	5.0
H(4)	196	737	3580	5.0
H(5)	−13	3093	4306	5.0
H(6)	518	5168	5039	5.0
H(7)	1293	4917	5095	5.0
H(Cp1)	2214	−570	1809	5.0
H(Cp2)	1634	−2637	1971	5.0
H(Cp3)	1668	−2756	3837	5.0
H(Cp4)	2273	−781	4834	5.0
H(Cp5)	2604	660	3588	5.0
H(Cp6)	850	3381	2311	5.0
H(Cp7)	686	845	1178	5.0
H(Cp8)	1393	234	642	5.0
H(Cp9)	1999	2433	1492	5.0
H(Cp10)	1639	4330	2492	5.0